The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 144, NO. 1 — CHICAGO, ILLINOIS — SEPTEMBER 2, 1950

COPYRIGHT, 1950, BY AMERICAN MEDICAL ASSOCIATION

EVALUATION OF CYTOLOGIC DIAGNOSIS OF LUNG CANCER

SEYMOUR M. FARBER, M.D.
ALLEN K. McGRATH Jr., M.D.
MORTIMER A. BENIOFF, M.D.
and
MILTON ROSENTHAL, M.D.
San Francisco

Since the pioneer report of Papanicolaou and Traut in 1943, most investigators have corroborated the application of cytologic technics to cancer diagnosis.[1] Malignant cells have been identified in secretions and exudates from most accessible tracts of the body including the respiratory tract.

In the first evaluations of cytologic diagnosis of lung cancer, patients with a high incidence of carcinoma were studied. A circumscribed impression of the sensitivity and reliability of cytologic diagnosis was gained. A more meaningful appraisal of this diagnostic technic can be obtained by study of its result in a large series of cases with varied pulmonary conditions, in which lung cancer entered the differential diagnosis only as a possibility.[2] Such a series is presented here, as are methods by which some of the pitfalls in evaluation and utilization of this technic may be avoided.

RESULTS OF EXAMINATIONS OF 2,066 PATIENTS

This report is a summary of experience for the past three years in examining the sputum and bronchial secretions of 2,066 patients by the Papanicolaou and Traut technic. A complete description of various normal, atypical and malignant cellular components found in sputum and bronchial secretions, with detailed instructions for utilizing technical procedures, may be found in a monograph.[3]

SOURCE AND DESCRIPTION OF CASES

The patients in table 1 represent a diversified patient population derived from many institutions and physicians, none primarily interested in the diagnosis and treatment of cancer. We have accepted specimens of sputum or bronchial secretions submitted to us from any patient with thoracic symptoms in whom there were suspicions of cancer, even if remote. Otherwise, there has been no selection of clinical material.

There have been the usual difficulties in tracing patients from scattered sources, but 1,758 of 2,066 patients (85 per cent) examined have been followed to a definite pathologic or clinical diagnosis. It is planned to follow all patients to a final diagnosis for a five year period.

A total of 6,281 specimens of sputum and bronchial secretions from 2,066 patients were submitted in four years. Patients examined by both methods totaled 208. Four hundred and fifty-seven patients were studied by a complete series of 5 sputum examinations.

From the total of 2,066 patients studied, positive cytologic diagnoses were made on 201 patients by examining sputum or bronchial secretions. Of these positive cytologic diagnoses, 176 were reported as definitely malignant and 25 as "suspicious for malignancy." In 9 patients, cells "inconclusive for malignancy" were reported and more specimens requested.

Pathologic proof of bronchogenic carcinoma was obtained in 125 of these 201 patients with positive cytologic diagnoses. Fifty patients had clinically diagnosed bronchogenic carcinoma; 22 had metastatic carcinoma to the lung, and 2 patients had clinically benign chest disease. Two positive reports were made on patients with pathologically proved benign conditions.[4] In none of these was the clinical status of the patient known to the cytologic diagnostician; in each case the cytologic diagnosis was made on the basis of the cellular criteria alone.

FACTORS INFLUENCING THE DIAGNOSTIC RESULTS OF CYTOLOGIC EXAMINATION

Our series of 241 patients with pathologically proved bronchogenic carcinoma was analyzed to determine the relation of cytologic diagnosis to the following factors.

A. Cell Type.—As shown in table 3, small cell undifferentiated carcinomas are detected only half as frequently as the differentiated epidermoid and adenocarcinomas. This is primarily due to the difficulty in distinguishing small undifferentiated carcinoma cells from "small round cells." Also, the characteristics of malignancy in small cells are difficult to determine accurately especially in the absence of many such cells in the smear.

Dr. McGrath is a trainee of the National Cancer Institute, Bethesda, Md.

From the Division of Medicine and the Department of Pathology, University of California School of Medicine, San Francisco Hospital and the San Francisco Department of Public Health.

1. Farber, S. M.; Benioff, M. A.; Frost, J. K.; Rosenthal, M., and Tobias, G.: Cytologic Studies of Sputum and Bronchial Secretions in Primary Carcinoma of the Lung, Dis. of Chest **14**: 5, 1948. Farber, S. M.; Benioff, M. A., and McGrath, A. K. Jr.: Diagnosis of Bronchogenic Carcinoma by Cytologic Methods, Radiology **52**: 511, 1949. Clerf, C. H., and Herbut, P. A.: Diagnosis of Bronchogenic Carcinoma by Examination of Bronchial Secretions, Ann. Otol., Rhin. & Laryng. **55**: 646, 1946. Papanicolaou, G. N., and Cromwell, H. A.: Diagnosis of Cancer of the Lung by the Cytologic Methods, Dis. of Chest **15**: 4, 1949. MacDonald, J. R., and Woolner, L. B.: Cytologic Examination of Sputum and Bronchial Secretions in Diagnosis of Bronchogenic Carcinoma, Surg., Gynec. & Obst. **88**: 5, 1949.

2. Liebow, A.; Lindskog, G., and Kleemer, W.: Cytologic Studies of Sputum and Bronchial Secretions in Diagnosis of Cancer of the Lung, Cancer **1**: 223, 1948.

3. Farber, S. M.; Rosenthal, M.; Alston, E. F.; Benioff, M. A., and McGrath, A. K., Jr.: Cytologic Diagnosis of Lung Cancer, Springfield, Ill., Charles C Thomas, Publisher, 1950.

4. In 1 patient with surgically proved primary lung abscess, abundant histocytes with mild nuclear disproportion were expectorated. The other patient showed pneumonitis as the only pulmonary disease at autopsy. Numerous hypercornified metaplastic squamous cells were expectorated. Both types of cells are entirely familiar now and have been seen frequently in sputum from patients with nonmalignant disease. Such experience indicates that, unlike many "laboratory tests," this method of examination becomes progressively more accurate.

B. Location of Lesion.—The site of the lesion may effect the concentration and accessibility of the exfoliated cells. The cytologic technic is of diagnostic value in many patients with lesions not visualized by the bronchoscopist.

TABLE 1.—*Source of Clinical Material*

	Cases	
	No.	%
San Francisco City and County Hospital	901	43
University of California Hospital	490	24
Pathologists (general hospitals)	186	9
County hospitals and sanatoriums	180	9
Government hospitals	100	5
Office patients	89	4
Stanford University Hospitals	21	1
Outside United States	9	..
Total	2,065	100

In 60 patients, the lesion was proved to be peripheral by surgery or autopsy studies. When examined by the cytologic technic, 36 had positive smears; 49 of the 60 patients were examined bronchoscopically without a single positive morphologic diagnosis.

C. Type of Examination.—Cytologic reports on the sputum of 196 of the 241 patients with proved bronchogenic carcinoma were returned. Malignant cells were found in 110 (57 per cent) of these patients.

Bronchoscopically obtained smears were examined in 113 of 241 patients with proved primary carcinoma of the lung, and in 40 (35 per cent) malignant cells were found.

When sputum is not available, cytologic studies may be made on aspirations of bronchial secretions or by lavage of the suspected site of cancer through the bronchoscope. Sputum, of course, is more easily obtained than bronchoscopic aspirations. At little

TABLE 2.—*Status of All Patients Studied Cytologically*

	Patients
A. Malignant Pulmonary Disease	503
Bronchogenic carcinoma (proved)	241
Bronchogenic carcinoma (clinical)	121
Cancer, metastatic to lung (proved)	39
Cancer, metastatic to lung (clinical)	81
Malignant lymphomata	21
B. Nonmalignant Pulmonary Disease	1,208
Tuberculosis	310
Inflammatory disease (pneumonitis)	240
Bronchiectasis	84
Cardiovascular disease	138
Abscess, pulmonary	44
Bronchitis	50
Infarct, pulmonary	33
Granuloma of lung, other than tuberculosis	24
Bronchial asthma	28
Neoplasms of lung (benign)	18
Pulmonary fibrosis of unknown cause	21
Pleural effusion (undetermined cause)	19
Empyema, pleural	8
Emphysema, pulmonary	24
Miscellaneous	167
C. Nonpulmonary Malignancy Without Parenchymal or Bronchial Invasion	47
D. Definitive Diagnosis not Established	308
Total	2,066

trouble or expense, repeated specimens of sputum may be secured to achieve greater accuracy. Most important, sputum is more likely to be utilized by the physician for studies on patients with minimal chest symptoms that do not lead to immediate bronchoscopy.

D. Number of Examinations.—A complete series of five sputum specimens each were examined in 130 of 241 patients with pathologically proved primary lung cancer. The cytologic diagnoses were positive in 90 per cent, indicating that the sensitivity of the cytologic technic increases as more specimens are examined. Of the 65 patients missed because of incomplete sputum studies, only one specimen was examined in 32 patients and only two, three or four specimens in the remaining 33. We believe it is essential to examine routinely five specimens of sputum, to request sputum examinations whenever bronchial smears are examined and found negative and to request repeated specimens when the cytologic findings are equivocal. A negative cytologic examination does not rule out the presence of cancer and must be correlated by the clinician with other findings.

E. Stage of Lesion.—In our series of 241 patients with proved bronchogenic carcinoma, 117 were surgically explored. In these patients, bronchoscopic biopsies were positive in 30 per cent and cytologic studies were positive in 54 per cent. In 33 of these patients who were operated on, cytologic evidence was the first morphologic proof of cancer and in 26 patients was the only preoperative morphologic proof of carcinoma.

Analysis of the 117 surgical patients shows that 69 resections were carried out. Seven patients survived

TABLE 3.—*Types of Cancer*

Cell Type	Number of Cases	Detected on Cytologic Examination	
		No.	%
Epidermoid	116	74	64
Adenocarcinoma	25	17	70
Undifferentiated	43	13	30
Unstated type	57	21	37
Total	241	125	

TABLE 4.—*Peripheral Lesions*

	Cytology					
	Bronchial		Sputum		Bronchoscopy	
Right:	Positive	2	Positive	15	Suspicious	5
	Negative	2	Negative	12	Negative	22
Left:	Positive	2	Positive	17	Suspicious	5
	Negative	0	Negative	11	Negative	17

without recurrence and are well at present, an average of eleven months after resection. Preoperative cytologic studies were positive in 4 of these 7 patients. An additional 16 patients survived pneumonectomy, and their cases are now being reviewed. In other words, of 241 patients with proved primary lung cancer, 23 are known to have a possibility of an eventual five year cure. This small survival may indicate that examinations are not instituted sufficiently early.

CRITICAL EVALUATION OF CYTOLOGIC DIAGNOSIS

Certain factors influence the results obtained by cytologic methods. These must be considered by both the cytologic diagnostician and the clinician who must properly evaluate the dependability of the diagnoses.

1. Reliability is the first objective of cytologic diagnosis.

Throughout our investigation we have emphasized reliability, often at the expense of sensitivity of diagnosis. We believe that in bronchogenic carcinoma a reliable diagnosis (absolute minimum of false positive diagnosis in a given series) that would justify operative intervention in the absence of other morphologic evidence would be of greatest value. The use of presumptive diagnoses with high sensitivity (few missed cases) to provoke further diagnostic procedures is another legitimate function of the cytologic method.

Almost absolute reliability can be obtained by rigid adherence to carefully determined cytologic criteria of malignancy. If suggestive cells, which are seen in many specimens, are reported as definitely malignant, a higher percentage of patients with bronchogenic carcinoma will be detected, but the number of false positive diagnoses also will be increased. We have often refrained from a definitive diagnosis because of remote but lingering doubt. If suggestive cells are reported as such, but not interpreted as unequivocally malignant, the positive diagnoses can be relied on almost 100 per cent.

In our series of reported cases we failed to diagnose an appreciable number of proved cancers of the lung. In 1,208 patients with benign chest diseases, the cytologic diagnosis was negative in 1,206. The only 2 pathologically proved false "suspicious" reports were rendered in the first year of our project. While we were studying 1,208 patients with benign chest conditions, only these 2 pathologically proved false positive diagnoses were rendered. The reliability of the method was established when extensive follow-up of positive cytologic diagnoses in a patient group containing this large proportion of control material failed to uncover any additional "false positive" reports.

2. Reliable cytologic diagnoses are based on objective application of criteria for cancer.

It has been our experience that the final decision of the cytologist is unavoidably influenced if the clinical status of the patient or the opinions of other members of the group are known to him. We believe that in every case the cytologic diagnosis should be rendered on the basis of precise morphologic criteria alone.

3. The sensitivity of cytologic diagnosis is directly related to the consistent application of technical procedures.

Technical procedures utilized in the cytologic work have an important bearing on the sensitivity of the method. At the outset, it is essential that technicians with adequate training (approximately 4 months) be available for careful screening of smears for atypical cells. The many technical difficulties [8] cannot be outlined here, but trained and intelligent technical personnel can work out problems of smearing, fixation, and staining as the material is handled. It is obvious that proper selection of particles for smearing, standardization of bronchoscopic aspirations, fixation and staining are necessary for a meaningful evaluation of the results. If the cell detail is obscured by improper technical preparation, the examination is without value. Analysis of those patients with proved bronchogenic cancer who were reported by our laboratory, on the basis of cytologic studies, as not having cancer in the first year showed that 55 per cent of the smears examined were unsatisfactory, owing to drying before fixation or scantiness of material. At the present time these slides would be reported as "unsatisfactory" rather than "negative." Improvement in the technical aspects of the method and examination of repeat specimens when unsatisfactory smears are presented for examination increase the efficiency and accuracy of the cytologic method.

4. The sensitivity of the procedure rises distinctly as the number of specimens increases.

When five or more specimens of sputum or bronchial secretions are examined, 90 per cent of the patients with pathologically proved bronchogenic cancer had positive cytologic diagnoses. This yield decreases to 55 per cent when fewer specimens are examined. By submitting or requesting specimens, the clinician and cytologic diagnostician can directly influence and increase the sensitivity and reliability of the technic.

5. Control patients with nonmalignant chest diseases should be included in all series.

In order to attain a broad experience and familiarity with the many possible variations which occur in cells from different types of pathologic conditions, as many diversified patients as possible should be included. Such varied clinical material would not only give the cytologic diagnostician familiarity with unusual cells but would also make possible a more realistic evaluation of the applicability of the cytologic technic to the general medical population than would be afforded by material with a preponderance of cancer. The goal—the exclusive association of certain cells with carcinoma—is more nearly approached. In addition, certain characteristics of malignant cells which were not impressive at first have proved to be entirely reliable. Detailed discussion of these characteristics is included in a previous publication.[8]

If the case material contains a preponderance of cancer, an exaggerated indication of the method's sensitivity may be obtained. If bizarre atypical cells are reported malignant by cytologic studies in patients with a large preponderance of cancer, the cytologist will achieve a high percentage of case finding but will have less opportunity to develop precise diagnostic criteria.

6. Complete follow-up of all patients to final diagnosis should be attempted.

An extensive follow-up of all patients is essential if errors in cytologic diagnosis are to be recognized and corrected and the over-all efficiency of the technic properly evaluated. It is extremely helpful to know the diagnoses of the many patients presenting equivocal cells in smear specimens. If it is known that various types of atypical cells are exfoliated from benign lesions, it will then become less difficult to distinguish these from malignant cells. It is evident that patients with positive cytologic diagnoses must be followed to check their reliability. Finally, if the negative cytologic diagnoses are not followed, patients with cancer undetected by the cytologic technic will be unrecognized and a false impression of the method's sensitivity may develop.

An illustration of this from our own experience showed that up to October of 1948, 500 patients had been examined and approximately 50 per cent followed to a definite diagnosis. At that time the apparent accuracy of the method was over 80 per cent. At the present time, after extensive follow-up, 85 per cent of 2,066 patients have had a definite diagnosis by clinical or pathologic study. Owing to the reporting of many cases of cancer missed by cytologic examination, the over-all sensitivity of case finding for the method is now 55 per cent. However, it should be emphasized that when an adequate study of five sputum specimens was examined, the case finding sensitivity of the method has remained about 90 per cent for the entire three year period.

7. A negative cytologic diagnosis must be carefully evaluated.

When the results of a complete cytologic examination are negative, cancer of the lung is not ruled out. The findings on each patient must be evaluated by the clinician. Repeat examinations may be made without delaying other indicated procedures.

There are many factors which may contribute to the failure of cytologic diagnosis in patients with lung

cancer. There may be interference with desquamation of cells because of the nature of the lesion. If the bronchus is stenotic, the secretions may not be expelled by cough or at bronchoscopy. Suppuration frequently associated with bronchogenic carcinoma may obscure the cells by simple dilution. In such patients we have found that cells occasionally may be demonstrated after antibiotics have been used to reduce the secondary infection.

8. Extensive experience is the most important single factor in cytologic diagnosis.

With the development of skill with this technic, both the reliability and the sensitivity of the results will improve. Reliability is dependent on adherence to continuously evaluated standards of criteria for cancer in smears. Various methods to obtain a knowledge of the bizarre appearances of malignant and benign cells in smears may be utilized: Direct smears of tumors and of benign epithelium may be fixed and stained and compared with the corresponding tissue section; bronchial secretions from known cancers may be obtained at autopsy and studied in the same manner; and sputum and bronchial secretions from proved cases of lung cancer and benign chest conditions may be studied. Finally, conditional diagnoses may be rendered for a period of time by the inexperienced cytologist on patients suspected to have pulmonary cancer.

At the same time, as cytologic criteria are developed, artifacts in cells due to fixing and staining which may simulate malignant characteristics should become familiar. These artifacts are less frequent in smears than in sections and are usually easily determined.[3] If the method of study and evaluation of results is that outlined above, the cytologist should obtain a wide experience with the confusing bizarre cells that occur in patients with benign chest conditions and be able to evaluate his facility with the method. The sensitivity for case finding increases as subtle cell abberations become familiar and their absence in nonmalignant pulmonary disease is learned.

COMMENT

It has been found that a positive cytologic diagnosis can be thoroughly reliable. The results of our experience with this diagnostic technic applied to patients with all types of pulmonary lesions in various locations and stages of growth have been outlined. It is considered a sensitive method, comparing favorably with and complementing other diagnostic aids. It is sufficiently simple, convenient and inexpensive for the patient and physician so that it may be utilized in the future as easily as a roentgenogram if laboratory facilities are available.

In our series of 241 pathologically proved cases of bronchogenic carcinoma, the first morphologic diagnosis was established by cytologic methods in 46 per cent. In many patients, a positive cytologic diagnosis was made weeks before other diagnostic procedures confirmed by pathologic studies the diagnosis of bronchogenic carcinoma. Only 7 patients surviving pneumonectomy for 4 months or more were included in our series. Of these, cytologic diagnoses were positive in 4. The value of this technic in detecting early bronchogenic carcinoma must be established in the future after much thorough investigative work.

We propose to evaluate this phase of the problem by utilizing routine screening procedures. Mass miniature roentgenologic surveys have opened a new field for the early diagnosis of chest disease. Although these surveys are utilized primarily for the detection of unsuspected pulmonary tuberculosis, it is known that many patients with lesions suggestive of bronchogenic cancer will be discovered. In our series, 70 per cent of the patients with positive cytologic diagnoses were discovered after cytologic examination of the first sputum specimen. Thus, from a practical point of view, a single cytologic study should be of great aid in screening patients with undiagnosed chest conditions.

We also urge the use of cytologic technics in any instance where the patient might have carcinoma of the lung, whether the initial symptoms are the development of recent cough, change in character of cough or sputum and suggestive roentgenographic findings. Any suspicion of cancer, especially in male patients over 40 years of age, should be investigated. At the present time at the San Francisco Hospital, we are attempting to investigate by routine cytologic examination any patient in this age group who enters with respiratory symptoms.

In conclusion, a strong word of warning is indicated. The reliability and sensitivity of the cytologic method can be readily attained by an experienced cytologist. We do not believe that such reliability can be attained without first having had considerable experience with the variations that occur among benign as well as malignant cells. We urge utmost caution in making positive diagnoses until these are justified by experience.

SUMMARY AND CONCLUSIONS

In four years, 2,066 patients were studied by cytologic examination of sputum and bronchial secretions. In 1,758 cases a definitive diagnosis was established. There were 362 patients with proved or clinically diagnosed bronchogenic carcinoma. One hundred and twenty patients with metastatic lung cancer were encountered in this group.

Positive cytologic diagnoses were rendered in 201 patients, and 1,865 negative diagnoses were made. The positive reports were made on patients with pathologically proved malignant disease, with the exception of two false suspicious diagnoses made on patients with pathologically proved benign diseases.

The over-all percentage of accuracy in our series of 241 patients with proved bronchogenic carcinoma was 55 per cent. When an adequate series of five sputum specimens was examined, the case finding sensitivity was 90 per cent in 130 patients.

The following factors should be considered in evaluating this diagnostic technic:

(*a*) Reliability is the first objective of cytologic diagnosis.

(*b*) Reliable cytologic diagnoses are based on objective application of criteria for cancer.

(*c*) The sensitivity of cytologic diagnosis is directly related to consistent application of technical procedures.

(*d*) The sensitivity of the procedure rises markedly as the number of specimens increases.

(*e*) Patients with nonmalignant chest diseases should be included in all series as a control.

(*f*) Complete follow-up of all patients to final diagnoses should be attempted.

(*g*) A negative cytologic diagnosis must be carefully evaluated.

(*h*) Extensive experience is the most important single factor in cytologic diagnosis.

The ultimate value of cytologic technics in the early diagnosis of primary lung cancer remains to be established by further investigative work.

A CLINICAL EVALUATION OF CERTAIN ANTIHISTAMINIC AND ANTISPASMODIC DRUGS IN PARKINSON'S DISEASE

ABRAHAM S. EFFRON, M.D.
and
PETER G. DENKER, M.D.
New York

James Parkinson [1] wrote in 1817: "Although, at present, uninformed as to the precise nature of the disease, still it ought not to be considered as one against which there exists no countervailing remedy. On the contrary, there appears to be sufficient reason for hoping that some remedial process may ere long be discovered, by which, at least the progress of the disease may be stopped." One hundred and thirty-three years later the truth of this observation and hope is still incompletely fulfilled. The results of therapy in parkinsonism have left a great deal to be desired in spite of considerable advances in knowledge of the anatomy and pathology of the central nervous system related to parkinsonism.

Many drugs have been tried and various procedures attempted since Parkinson recommended: "At whatever period of the disease it might be proposed to attempt a cure, blood should be first taken from the upper part of the neck, unless contraindicated by any particular circumstance. After which vesicatories should be applied to the same part, and a purulent discharge obtained." The generally accepted treatment has for some time been the use of atropine, scopolamine (hyoscine) hydrobromide or stramonium. In a variable number of patients, these solanaceous drugs could generally be depended on to give some measure of relief. Other forms of drugs for oral or parenteral administration have been tried and have fallen into disuse. Such medicaments as quinine, neostigmine (prostigmin®) bromide, iodides, magnesium sulfate, amphetamine (benzedrine®), snake venom, salicylates and phenobarbital, as well as vitamins of all types and combinations, have had their moments of enthusiastic acceptance but have not stood the test of time as therapeutic agents. In the past decade neurosurgeons have also attempted to help these unfortunate persons with various procedures but, as yet, without convincing results. Such advocates as Fulton, Putnam, Bucy, Delmas-Marsalet, Jackson, Browder, Klemme [2] and Ebin [3] have all devised individual approaches, but the diversity of these various attempts is in itself an admission of the fact that, as yet, no surgical procedure has provided the ultimate therapeutic answer. Today, we are still searching for that "remedial process" in the hope that relief can be achieved in this disease.

Antihistaminic compounds have been among the more recent drugs tried in the therapy of parkinsonism. McGavack, Elias and Boyd [4] reported improvement with diphenhydramine (benadryl®) hydrochloride, an ethanolamine derivative, in 3 of 4 cases of arteriosclerotic parkinsonism. Budnitz [5] obtained improvement in 8 patients with arteriosclerotic parkinsonism with diphenhydramine hydrochloride, but these patients derived no benefit from tripelennamine (pyribenzamine®) hydrochloride, a derivative of ethylenediamine. Ryan and Wood [6] reported "therapeutically effective" results with diphenhydramine hydrochloride in their series of 40 cases. Blumberg and Dattner [7] compared diphenhydramine hydrochloride and phenindamine (thephorin®) tartrate (2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene hydrogen tartrate), which is chemically unrelated to the other histamine antagonists, in 25 cases and found subjective improvement with both drugs, but particularly with phenindamine tartrate. Berger [8] more recently reported improvement in 13 of 24 cases with phenindamine tartrate, and in about three fourths of these cases with diphenhydramine hydrochloride, but he stated that phenindamine tartrate provided a greater degree of improvement.

Doshay and Constable,[9] using artane® (3-[1-piperidyl]-1-phenyl-1-cyclohexyl-1-propanol hydrochloride), one of the newer synthetic antispasmodic compounds, reported improvement in 89 of 117 patients, an incidence of 76.1 per cent. Similarly, Corbin [10] obtained benefit in 80 of the 104 patients he treated with artane,® an incidence of 77 per cent. Schwab and Tillman [11] found artane® comparatively ineffective alone, but of therapeutic value when combined with other medication.

Stephen and Chandy [12] reported temporary improvement with the intravenous administration of a 10 per cent solution of mephenesin (tolserol,® myanesin®)—an alpha-substituted ether of glycerin—in 3 cases of paralysis agitans. In these patients this drug abolished the involuntary movements for 30 to 45 minutes. Hunter and Waterfall [13] obtained similar results by the same method. Schlesinger, Drew and Wood [14] administered intravenously a 2 per cent solution of mephenesin in isotonic sodium chloride solution and obtained reduction of rigidity as well as of tremor. Berger and Schwartz [15] reported reduction of ridigity and tremor with this muscle relaxant given orally; but results were not so good as by the intravenous route.

PROCEDURE AND FINDINGS

The case material comprised 80 unselected patients with Parkinson's disease. Of these, 38 were of the postencephalitic, 21 of the arteriosclerotic and 14 of the idiopathic type, with 7 being classified as syphilitic, malarial or traumatic. Most of these patients were in a fairly well advanced stage of the disease. In fact, there were only 8 subjects with only one limb involved

From the Neurological Service of Dr. Foster Kennedy, Bellevue Hospital (Cornell Division), New York. Resident Neurologist (Dr. Effron) and Asociate Attending Neurologist (Dr. Denker).

Lederle Laboratories, division of the American Cyanamid Company, supplied artane®; Parke, Davis & Company supplied benadryl®; Eli Lilly & Company supplied histadyl®; Ciba Pharmaceutical Products, Inc., supplied pyribenzamine®; Hoffmann-La Roche, Inc., supplied thephorin®; and E. R. Squibb & Sons supplied tolserol.®

1. Parkinson, J.: An Essay on the Shaking Palsy, London, Whittingham & Rowland, 1817.
2. Klemme, R. M.: Surgical Treatment of Dystonia, with Report of 100 Cases, A. Research Nerv. & Ment. Dis., Proc. (1940) **21**: 596-601, 1942.
3. Ebin, J.: Combined Ventral and Lateral Pyramidotomy in the Treatment of Paralysis Agitans, to be published.
4. McGavack, T. H.; Elias, H., and Boyd, L. J.: Some Pharmacological and Clinical Experiences with Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl), Am. J. M. Sc. **213**:418-434 (April) 1947.
5. Budnitz, J.: The Use of Benadryl in Parkinson's Disease: A Preliminary Report of 8 Cases, New England J. Med. **238**: 874-875 (June 17) 1948.
6. Ryan, G. M. S., and Wood, J. S.: Benadryl in the Treatment of Parkinsonism: Results in 40 Cases, Lancet **1**: 258-259 (Feb. 12) 1949.
7. Blumberg, A. G., and Dattner, B.: Benadryl and Thephorin in the Treatment of Advanced Parkinsonism, to be published.
8. Berger, F. M.: The Treatment of Paralysis Agitans with Thephorin, New York State J. Med. **49**: 1817-1820 (Aug. 1) 1949.
9. Doshay, L. J., and Constable, K.: Artane Therapy for Parkinsonism: Preliminary Study of Results in 117 Cases, J. A. M. A. **140**: 1317-1322 (Aug. 27) 1949.
10. Corbin, K. B.: Trihexyphenidyl: Evaluation of New Agent in Treatment of Parkinsonism, J. A. M. A. **141**: 377-382 (Oct. 8) 1949.
11. Schwab, R. S., and Tillman, W. R.: Artane in the Treatment of Parkinson's Disease: A Report of Its Effectiveness Alone and in Combination with Benadryl and Parpanit, New England J. Med. **241**: 483-485 (Sept. 29) 1949.
12. Stephen, C. R., and Chandy, J.: Clinical and Experimental Studies with Myanesin (Preliminary Report), Canad. M. A. J. **57**: 463-468 (Nov.) 1947.
13. Hunter, A. R., and Waterfall, J. M.: Myanesin in Hyperkinetic States, Lancet **1**: 366-367 (March 6) 1948.
14. Schlesinger, E. B.; Drew, A. L., and Wood, B.: Clinical Studies in the Use of Myanesin, Am. J. Med. **4**: 365-372 (March) 1948.
15. Berger, F. M., and Schwartz, R. P.: Oral "Myanesin" in Treatment of Spastic and Hyperkinetic Disorders, J. A. M. A. **137**: 772-774 (June 26) 1948.

who were able to carry on well with their usual functions. Of the remaining 72 patients, 35 had more than one limb involved, with considerable functional impairment, and 37 were unable to carry on functionally or were bedridden. Not all of these cases were available at the beginning of the study.

As each patient presented himself, all medication heretofore used was discontinued in order to establish a base line of his status. Then one of the following drugs was administered: artane,® diphenhydramine hydrochloride, methapyrilene (histadyl®) hydrochloride, scopolamine hydrobromide, tripelennamine hydrochloride, phenindamine tartrate or mephenesin. After the effect of one of these compounds had been evaluated and if results were favorable, the patient was placed on placebo medication simulating in size, color and shape the preceding medicament. Placebo medication was continued until the patient returned approximately to the base line previously established for him. Then another of the aforementioned drugs was used, again followed by placebo medication, to be subsequently replaced by a third drug and so on in order to draw comparative results. Rather than to employ the same compound initially in each patient, the choice of the first drug to be used depended on the time when the patient entered into the study. By the same token, a subject who was included at a later stage of the project was started on the particular drug then employed. As the work progressed, combinations of drugs were used also.

The original plan called for the administration of each compound for a period of one month during which time the dose was to be gradually increased. It was anticipated that some patients would not tolerate a given drug and that others would be lost from observation prior to completion of this program, thus reducing appreciably the total number of comparative observations.

The appraisal of therapeutic results in Parkinson's syndrome is open to a wide range of interpretation, since the reaction of patients is predicated on many factors, some of which are beyond the rigid control of the examiner. Notwithstanding, it was attempted to assess results as objectively as possible. Thus, relief from symptoms was neither suggested nor promised to the patients, who were encouraged to describe their responses spontaneously. Each patient was given a general physical and neurologic examination initially. Reexaminations were carried out once a week, and urinalyses and hemograms [16] were repeated at frequent intervals. Changes in posture, gait, agility, rigidity, tremor, speech, salivation and functional activities were carefully recorded. The degree of positive responses was classified as slight, moderate or marked improvement. Admittedly, this classification largely reflects the examiner's subjective appraisal, but a disease with such protean clinical findings as Parkinson's disease almost defies the establishment of objective criteria for improvement. Negative responses included no improvement, aggravation and toxic manifestation.

Artane.®—Artane® was studied in 48 patients. Initially each subject received 1 mg. three times a day, and this was gradually increased until a maximum of 5 mg. four times a day was given at the beginning of the fourth week. Thirty-one patients derived some degree of benefit from artane,® an incidence of improvement of 64.5 per cent. (Chart 1 indicates the degrees of improvement obtained with this drug and with the other compounds and combinations studied.) Of these 31 subjects, 3 were classified as markedly, 11 as moderately and 17 as slightly improved. Negative responses were recorded for 17 patients, or 35.5 per cent. Of these, there was no improvement in 9 instances, exaggeration of tremor in 1 and toxic manifestations, necessitating discontinuance of the drug, in 7. The latter included 2 patients with a generalized pruritus, 3 with nausea and vomiting and 2 with psychosis characterized by confusion and memory impairment. These toxic effects cleared the day after the administration of the drug was discontinued.

Diphenhydramine Hydrochloride. — Diphenhydramine hydrochloride was tried in 57 patients. Initially each subject was given 50 mg. three times a day, and this was gradually increased to 100 mg. four times a day. A daily dose of 400 mg. was administered during the fourth week. Forty-two patients were benefited (73.7 per cent). Of these, 7 were classified as markedly, 15 as moderately and 20 as slightly improved (chart 1). Negative responses were recorded for 15 patients (26.3 per cent). Of these, there was no improvement in 7 patients, exaggeration of symptoms and immobility in 1 and toxic manifestations requiring withdrawal of the drug in 7. The last included excessive drowsiness in 3 and gastrointestinal irritation in 4 patients.

Methapyrilene Hydrochloride.—Methapyrilene hydrochloride was administered to 38 patients. In the beginning, each patient received a total daily dose of 150 mg. in three divided doses.

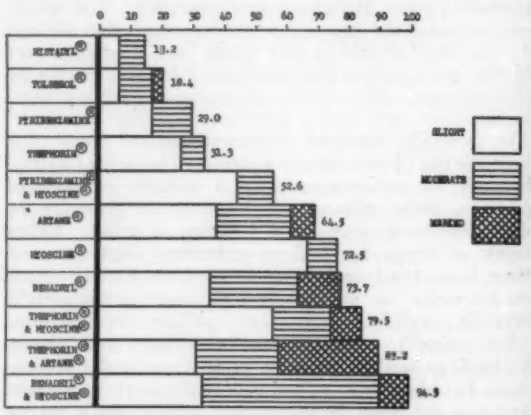

Chart 1.—Incidence and degree of improvement of patients with parkinsonian disease who received various antihistaminic and antispasmodic drugs and combinations thereof. In charts 1 and 2 the white areas indicate slight improvement; the diagonally lined areas, moderate improvement, and the crosshatched areas, marked improvement; the top line of figures represents percentage of patients improved.

This was gradually increased to 100 mg. four times a day, and this amount was continued during the fourth week. Five patients were recorded as showing positive responses, an incidence of improvement of 13.2 per cent. Of these, 3 were classified as moderately and 2 as slightly improved (chart 1). The negative responses (33 patients, or 86.8 per cent) included no improvement in 26, aggravation of symptoms in 6 and drowsiness warranting discontinuance of the drug in 1 patient.

Scopolamine Hydrobromide.—Scopolamine hydrobromide was given to 51 patients. The initial dosage was 1/200 grain (0.3 mg.) three times a day, and this was gradually increased at weekly intervals to 1/50 grain (1.2 mg.) four times a day. Thirty-seven patients derived some degree of benefit, an incidence of improvement of 72.5 per cent. Thirty-three were classified as slightly and 4 as moderately improved (chart 1). Negative responses were recorded for 14 patients (27.5 per cent). Of these, there was no improvement in 12, and 2 were unable to continue with the drug because of visual disturbances.

Tripelennamine Hydrochloride.—Tripelennamine hydrochloride was tried in 38 patients. The initial dose was 50 mg. three times a day and the maximum daily dose 400 mg. in four divided doses. Eleven patients, or 29 per cent, were benefited, with 5 classified as moderately and 6 as slightly improved (chart 1). Negative responses were recorded in 27 patients, or 71

16. Dr. I. Silberman, Chief of Laboratories of the Out-Patient Department, Bellevue Hospital, made the urinalyses and the blood cell counts.

per cent. Of these, there was no improvement in 16, exacerbation in 8, and there were toxic manifestations requiring discontinuance of the drug in 3 patients. Among the last 3 was a case of psychosis characterized by visual hallucinations and paranoid ideas.

Phenindamine Tartrate.—Phenindamine tartrate was administered to 48 patients. At first each patient received 25 mg. three times a day, and this was increased to a daily dose of 400 mg. given in four divided doses. Fifteen patients, or 31.3 per cent, were benefited, with 3 classified as moderately and 12 as slightly improved (see chart 1). Negative responses were found in 33 patients, or 68.7 per cent. Of these, there was no improvement in 28, and there were untoward symptoms requiring discontinuance of the drug in 5. Two of the latter patients were "nervous and agitated" and unable to sleep, 2 became excessively sleepy and 1 had nausea and vomiting. In addition, 7 patients complained of constipation, but they continued taking the drug according to plan.

Mephenesin.—Mephenesin was administered to 38 patients. The initial oral dose was 0.5 Gm. three times a day, and this was gradually increased for the majority of subjects to as much as 2 Gm. every three hours. Seven patients, or 18.4 per cent, obtained improvement; this was marked in 1, moderate in 4 and slight in 2 (chart 1). Negative responses were recorded in 31 (81.6 per cent), including no improvement in 23, feeling of increased rigidity in 2 and toxic symptoms of nausea and vomiting in 6 patients, most of whom were in the arteriosclerotic group. The intravenous use of mephenesin in 6 patients was not attended by a greater degree of improvement than the oral administration. An oculogyric crisis developed in one of these patients after 4,000 mg. of mephenesin had been administered by intravenous drip.

Diphenhydramine Hydrochloride and Scopolamine Hydrobromide. — Diphenhydramine hydrochloride and scopolamine hydrobromide were given to 36 subjects in varying doses up to the maximum previously noted for each drug. The patients, 31 of whom had previously received diphenhydramine hydrochloride alone or scopolamine hydrobromide alone, were so selected as not to include those who had derived marked benefit from diphenhydramine hydrochloride. Thirty-four patients (94.5 per cent) receiving the combined medication were classified as showing positive responses, the degree of improvement being marked in 3, moderate in 19 and slight in 12 (chart 1). In the two remaining patients the addition of scopolamine hydrobromide to diphenhydramine hydrochloride increased the tremor. One of the patients markedly improved was a 54 year old woman with severe immobility, drooling and inability to swallow or talk as a result of recent bilateral cerebrovascular accidents.

Tripelennamine Hydrochloride and Scopolamine Hydrobromide.—Tripelennamine hydrochloride and scopolamine hydrobromide were used in 19 patients. Only 10 subjects (52.6 per cent) showed improvement, which was classified as moderate in 2 and slight in 8 (chart 1). There was no change in the condition of the remaining 9 patients (47.4 per cent). One woman, who had only slight improvement with scopolamine hydrobromide and none with tripelennamine hydrochloride, improved to such an extent with the combined use of these drugs that she was able to resume her household duties.

Phenindamine Tartrate and Artane.®—Phenindamine tartrate and artane® were tried in 27 patients, all of whom had previously received phenindamine tartrate or artane® alone. They were so selected as not to include patients who had shown marked improvement with either drug alone. The total daily dose ranged from 100 to 200 mg. of phenindamine tartrate and from 8 to 10 mg. of artane,® and this was given in four equal doses. The incidence of improvement was 85.2 per cent with 8 patients deriving marked, 7 moderate and 8 slight improvement (chart 1). Negative responses were recorded in 4 patients (14.8 per cent). Of these, there was no change in 1 and nausea in 3, requiring discontinuance of the drugs.

Phenindamine Tartrate and Scopolamine Hydrobromide.—Phenindamine tartrate and scopolamine hydrobromide were evaluated in 34 patients who had previously received the two drugs separately. Every subject received a maximum daily dose of 400 mg. of phenindamine tartrate and 4/50 grain (4.8 mg.) of scopolamine hydrobromide in four equal doses. Twenty-seven subjects of the group were improved, an incidence of 79.5 per cent. The degree of improvement was recorded as marked in 3, moderate in 6 and slight in 18. A negative response was recorded for 7 patients (20.5 per cent); of these there was no improvement in 5 and aggravation of symptoms in 2.

Urinalyses and hemograms revealed no untoward effects on renal function or the hematopoietic system from any of the drugs used.

COMMENT

In comparing the over-all results obtained with the individual compounds it becomes apparent that methapyrilene hydrochloride and mephenesin were the least effective; that both tripelennamine hydrochloride and phenindamine tartrate helped approximately one third of the patients, and, finally, that artane,® scopolamine hydrobromide and diphenhydramine hydrochloride were of value in varying degrees in about 70 per cent of the cases.

Of the combinations used, tripelennamine hydrochloride and scopolamine hydrobromide resulted in improvement in approximately one half of the patients receiving these two drugs conjointly. In contrast, the incidence of improvement with phenindamine tartrate and sco-

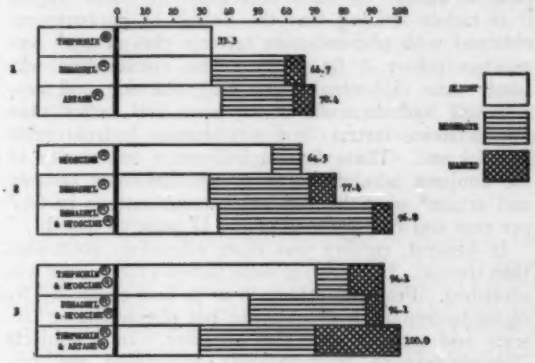

Chart 2.—Comparative findings in three groups of patients with parkinsonian disease. Figure 1 shows the incidence and degree of improvement of 27 patients receiving artane,® benadryl® and thephorin.® Figure 2 gives the incidence and degree of improvement for 31 patients receiving hyoscine,® benadryl® and a combination of both. Figure 3 shows the incidence and degree of improvement of 17 patients receiving thephorin® and hyoscine,® benadryl® and hyoscine,® thephorin® and artane.®

polamine hydrobromide, phenindamine tartrate and artane,® or diphenhydramine hydrochloride and scopolamine hydrobromide ranged from about 80 per cent to 95 per cent. It is seen in chart 1 that the incidence of marked improvement was highest in the group receiving phenindamine tartrate and artane.®

Admittedly, such comparative data have limited validity in view of the small numbers of cases studied and since the individual groups do not necessarily comprise identical patients.

More strictly comparable results are obtained by appraisal of the merits of drugs in trials performed in identical cases. Chart 2 records graphically such results in patients grouped together from the entire case material in such a manner that each group comprises subjects all of whom received several of the drugs studied or combinations thereof. Thus figure 1 represents the incidence of improvement recorded for 27 patients, all of whom received artane,® diphenhydramine hydrochloride and phenindamine tartrate; figure 2 represents comparative results attending the use of scopolamine hydrobromide, diphenhydramine hydrochloride

and a combination of both in 31 patients, and, finally, figure 3 portrays the incidence of favorable results in 17 subjects in whom combinations of phenindamine tartrate and artane,* diphenhydramine hydrochloride and scopolamine hydrobromide, and phenindamine tartrate and scopolamine hydrobromide were tried.

It can be seen from figure 1 of chart 2 that diphenhydramine hydrochloride and artane* were almost equally effective; in fact diphenhydramine hydrochloride was more effective than artane* in 10 cases (37.03 per cent), and artane* was more effective than diphenhydramine hydrochloride in 9 cases (33.3 per cent). Phenindamine tartrate alone was comparatively ineffective. In the group represented in figure 2, diphenhydramine hydrochloride plus scopolamine hydrobromide was more beneficial than scopolamine hydrobromide in 27 cases (87.1 per cent) and more beneficial than diphenhydramine hydrochloride in 11 cases (33.3 per cent). It appears from chart 2 that the incidence of success obtained with the conjoint administration of phenindamine tartrate and artane* was highest while the combination of phenindamine tartrate and scopolamine hydrobromide and of diphenhydramine hydrochloride and scopolamine hydrobromide proved beneficial in almost the same percentage of cases. Again it is rather striking that the degree of improvement obtained with phenindamine tartrate plus artane* was greatest (chart 2, figure 3). This combination was better than diphenhydramine hydrochloride and scopolamine hydrobromide in 11 cases and better than phenindamine tartrate and scopolamine hydrobromide in 13 cases. These figures indicate a superiority of the conjoint administration of phenindamine tartrate and artane* over the two other combinations in 64.7 per cent and 76.5 per cent of the 17 patients tested.

In general, rigidity was more effectively controlled than tremor. However, in some patients the tremor was abolished. Festination seemed to be best controlled by diphenhydramine hydrochloride, but phenindamine tartrate and artane* were also effective. In 5 subjects diphenhydramine hydrochloride diminished the frequency and duration of oculogyric crises. Scopolamine hydrobromide was more effective in controlling excessive salivation than any of the other compounds. Diphenhydramine hydrochloride, phenindamine tartrate and artane* checked the profuse perspiration of some patients satisfactorily. Blurring of vision, so frequently encountered with scopolamine hydrobromide, was not observed with the other drugs. Diphenhydramine hydrochloride produced drowsiness only in a comparatively small number of patients, although it has been reported in other disorders to be a frequent undesirable side effect.

In view of the great divergence in response of patients with Parkinson's disease to the individual medicaments available for treatment, it would appear important to compare the effect of a number of drugs or combinations of drugs in order to provide each subject with the medication most effective for his particular case.

SUMMARY AND CONCLUSIONS

The comparative effects of artane,* diphenhydramine (benadryl*) hydrochloride, methapyrilene (histadyl*) hydrochloride, scopolamine hydrobromide, tripelennamine (pyribenzamine*) hydrochloride, phenindamine (thephorin*) tartrate, mephenesin (tolserol*) and combinations of some of these drugs were studied in 80 unselected patients with Parkinson's disease. Results were as follows:

1. Methapyrilene hydrochloride and mephenesin were the least effective.
2. Tripelennamine hydrochloride and phenindamine tartrate helped about one third of the patients.
3. Artane,* scopolamine hydrobromide and diphenhydramine hydrochloride were of value in approximately 70 per cent of the cases.
4. Of the combinations used, tripelennamine hydrochloride and scopolamine hydrobromide resulted in improvement in about one half of the patients.
5. Best results were obtained with phenindamine tartrate and artane,* phenindamine tartrate and scopolamine hydrobromide and diphenhydramine hydrochloride and scopolamine hydrobromide. Eighty to ninety-five per cent of the patients derived benefit from these combinations. However, the degree of improvement was greatest with phenindamine tartrate plus artane.*

CONGENITAL PULMONARY STENOSIS WITH INTACT VENTRICULAR SEPTUM

WILLIS J. POTTS, M.D.
STANLEY GIBSON, M.D.
WILLIAM L. RIKER, M.D.
Chicago
and
C. R. LEININGER, M.D.
San Rafael, Calif.

Pulmonary stenosis is one of the most important of the congenital malformations of the heart. It occurs most frequently in conjunction with a defect of the ventricular septum, dextroposition of the aorta and hypertrophy of the right ventricle (tetralogy of Fallot). It occurs also in tricuspid atresia in which there is a defect of the auricular septum and usually a defect of the ventricular septum with rudimentary right ventricle. Congenital pulmonary stenosis also occurs with intact ventricular septum. In the majority of these cases, there is an open foramen ovale. Cyanosis depends on the amount of blood shunted from right to left through the foramen ovale and on the degree of pulmonary stenosis. If there is no shunt, cyanosis is absent.

In the tetralogy of Fallot and tricuspid atresia, the patient's condition may be much improved by subclavian-pulmonary [1] or aortic-pulmonary anastomosis,[2] which permits a greater flow of blood to the lungs. In congenital pulmonary stenosis with intact ventricular septum, these operations are of little benefit.

In the tetralogy of Fallot there is in the great majority of instances stenosis of the infundibulum of the right ventricle. In pulmonary stenosis with intact ventricular septum the stenosis is usually valvular in type. The latter condition permits direct approach to the pulmonary valve. Brock [3] has made a distinct contribution by inserting a valvulotome through the wall of the right ventricle and incising the valve.

We wish to report 4 cases in which pulmonary valvulotomy was done. We feel that they are of interest because of the early age of 3 of the patients, the some-

From The Children's Memorial Hospital, Chicago.
This study was aided by the Otho S. A. Sprague Laboratory and the Florence Olmstead Memorial Fellowship of the Women's Faculty Club of Northwestern University.

1. Blalock, A., and Taussig, H. B.: The Surgical Treatment of Malformations of the Heart in Which There Is Pulmonary Stenosis or Pulmonary Atresia, J. A. M. A. **128**: 189 (May 19) 1945.
2. Potts, W. J.; Smith, S., and Gibson, S.: Anastomosis of the Aorta to a Pulmonary Artery in Certain Types of Congenital Heart Disease, J. A. M. A. **132**: 627 (Nov. 16) 1946.
3. Brock, R. C.: Pulmonary Valvulotomy for the Relief of Congenital Pulmonary Stenosis; Report of 3 Cases, Brit. J. Surg. **1**: 1121 (June 12) 1948

what different technic from that employed by Brock and others, the remarkably uneventful convalescence and the striking improvement following operation.

The symptoms and signs vary considerably from those encountered in the tetralogy of Fallot and tricuspid atresia. There may be dyspnea and marked decrease of exercise tolerance with relatively little cyanosis. The heart is enlarged. There is usually a systolic murmur, often accompanied with a thrill at the base of the heart. Pulsation of the liver is frequently present. The fluoroscopic and roentgenographic examinations reveal enlargement of the right ventricle. The lung fields are clear. Inasmuch as poststenotic dilatation of the pulmonary artery is usually present, the pulmonary artery segment is usually prominent. Since the roentgenograms taken in the anteroposterior position were so nearly alike in all cases only one print of patient 2 is reproduced (fig. 1). The electrocardiogram shows right ventricular hypertrophy with high, sharp waves in lead 2, and intraventricular block may be present. Cardiac catheterization reveals much increased pressure in the right ventricle with abnormally low pressure in the pulmonary artery. The angiocardiogram fails to show an overriding of the aorta. The dye remains abnormally long in the right ventricle.

In 3 of the cases here presented, neither cardiac catheterization nor angiocardiography was carried out because of the age of the patients and their serious condition. We realized that we were on precarious ground in making the diagnosis, yet the lung fields were clear

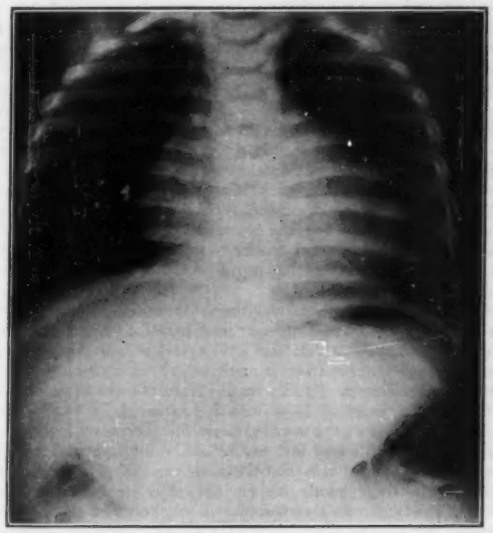

Fig. 1 (case 2).—Roentgenogram showing avascular lung fields, enlargement of the heart and prominence of the pulmonary artery segment.

and there was prominence of the pulmonary artery segment. The patients were going rapidly downhill, and we felt justified in attempting to relieve their condition.

THE VALVULOTOME

In 1948 Brock introduced a logical method of direct attack on the stenotic valve in patients having pulmonary stenosis with intact ventricular septum. The valvulotome used by him consists of a gently curved shaft to which is attached a diamond-shaped blade on the end of which is a small blunt probe. The advancing edges are sharp; the retreating edges are blunt. The instrument is made in graded sizes to meet variations in size of the pulmonary artery. Since the valvulotome must be introduced through the right ventricle it is obvious that the wound in the heart muscle will be as large as the diamond-shaped cutting blades.

In anticipation of an operation on a little child, a slightly different valvulotome was devised for us with the idea of decreasing the size of the wound in the heart and consequently lessening hemorrhage and

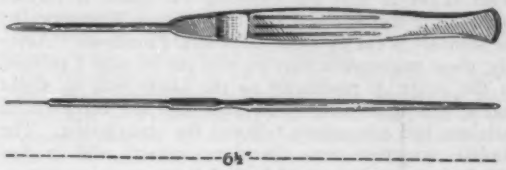

Fig. 2.—Valvulotome.

arrhythmia. A sharp cataract-type of knife blade was fashioned on a round shaft of steel, which, in turn, was attached to an ordinary knife handle for easy manipulation (fig. 2).[4] The rounded shaft of the knife is of such size that it will snugly fit the hole in the wall of the ventricle made by the blade and thus prevent loss of blood. This valvulotome, or knife, was tried on a number of dogs and found to be satisfactory. The knife could be introduced into the heart without much trauma and consequently without too much cardiac arrhythmia. Loss of blood was minimal. This knife has been used on 4 patients with isolated valvular stenosis with rather spectacular results. The following technic has been used with minor variations.

OPERATION

Preoperative medication consisting of morphine sulfate and atropine sulfate in appropriate doses is given one hour before operation. (For example, the 14 month old child [case 2] received $\frac{1}{360}$ grain [1.4 mg.] of morphine sulfate and $\frac{1}{300}$ grain [0.2 mg.] of atropine sulfate.) The patient is anesthetized in the supine position with ether and cyclopropane. An intratracheal tube is introduced. The patient is then raised to a semilateral position by sand bags placed beneath the left shoulder and hip.

A curved subpectoral incision is made on the left side, and the chest is opened through the third interspace. The second and third ribs are cut near the sternal margin. If more room is needed the fourth rib is similarly cut.

The pericardial sac is opened by a tiny incision (1 mm.) and approximately 5 cc. of 1 per cent procaine hydrochloride is introduced and allowed to bathe the heart for about three minutes to lessen its irritability. The pericardial sac is then widely opened well upward over the base of the heart to expose completely the pulmonary artery. The overlying phrenic nerve is retracted laterally or medially, whichever seems more feasible. If irregularities occur when the right ventricle is touched with a hemostat, more procaine is sprayed over the heart. Approximately 2 cc. of 1 per cent procaine hydrochloride solution is injected with a fine needle into the wall of the right ventricle over the area where the holding sutures are to be placed and where the valvulotome is to be inserted. Two 00000 Deknatel sutures, each on an atraumatic needle, are placed about 1 cm. apart in the wall of the right ventricle about 1.5

4. Instrument made by Bruno Richter, 843 Duane Street, Glen Ellyn, Ill.

cm. below the origin of the pulmonary artery to steady the heart and to control possible bleeding. The razor-sharp knife is now gently thrust through the wall of the ventricle at a very acute angle (fig. 3). The sharp edge of the knife is directed toward the lumen of the artery. With the left forefinger on the pulmonary artery as a guide, the blade of the knife is easily felt and directed through the base of the obstructing membrane close to the inner side of the pulmonary artery. With slight to and fro motions, the blade is carried through the stenotic veil into the lumen. Theoretically, the stenosis is cut by three such radial incisions. Actually, these maneuvers were carried out in only 1 patient. In the other 3, resistance to the blade was so slight that it was impossible to be sure that the three radial incisions had adequately relieved the obstruction. The filmlike structure was therefore incised with a few added thrusts. It seemed logical that excessive cutting

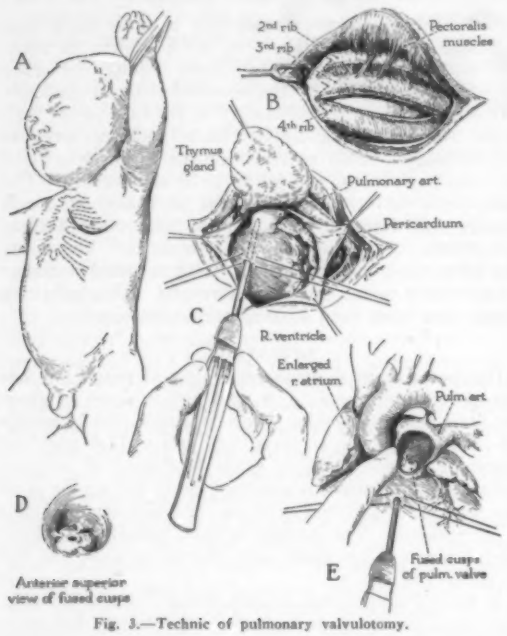

Fig. 3.—Technic of pulmonary valvulotomy.

of the obstruction was preferable to inadequate relief of the stenosis, even though more regurgitation might follow. Increased pressure in the pulmonary artery, easily discernible to the palpating finger, should be demonstrable before it is decided that the stenosis has been properly relieved. (A sudden rise in intrapulmonary pressure in a water manometer connected by needle to the pulmonary artery and/or elevation of the oxygen content of the blood as shown by oximeter are confirmatory of relief of the stenosis [case 4].)

A deep stitch of 00000 Deknatel silk on an atraumatic needle is now placed through the heart muscle close to the rounded shaft of the valvulotome and drawn up snugly and tied as the valvulotome is withdrawn. Although one stitch in the heart muscle controlled all bleeding in each case, a second stitch was added in three cases.

The pericardium is closed loosely with fine interrupted silk sutures, an opening at least 1 cm. long being left near the apex for the escape of pericardial fluid into the pleural cavity. A de Pezzer catheter, with all but a flange removed, is drawn from the inside out through the fifth interspace for drainage. The lung is expanded. The ends of the ribs are apposed, and the wound is closed in layers, running sutures of surgical gut being used for the muscles and silk for the skin. While the lung is held fully expanded by the anesthetist, the drainage tube is clamped. The patient is returned to an oxygenated crib. The drainage catheter is connected with a water seal bottle. Crystalline procaine penicillin G in 300,000 unit doses is given twice daily for five to seven days.

REPORT OF CASES

Case 1.—D. E., a white boy, weighing 7 pounds 5 ounces (3,317 Gm.), was admitted to Children's Memorial Hospital (Chicago) on Dec. 3, 1949, at the age of 4 days, with a history of cyanosis appearing at the age of 36 hours. The infant had to be maintained continuously in oxygen.

Physical examination revealed no cyanosis at rest, mild cyanosis when crying. The heart did not appear to be enlarged. A grade 3 blowing systolic murmur was best heard in the second left interspace. The second pulmonic sound was moderately increased and was narrowly split.

Laboratory examination revealed a red blood cell count of 5,670,000 per cubic millimeter and a hemoglobin count of 16.5 Gm. per hundred cubic centimeters. Routine roentgenographic and fluoroscopic examination revealed slightly decreased vascularity of the lung fields with moderate enlargement of the inflow and outflow tracts of the right ventricle. The pulmonary artery segment was rather prominent in the anteroposterior view. The pulmonary window was poorly visualized. The electrocardiogram showed a definite right heart strain with rather tall and peaked P waves in lead 2.

Pulmonary valvular stenosis with an interatrial septal defect seemed the most likely diagnosis. Since the infant could not live out of oxygen, operation was advised. The child was now 23 days old.

The operation was performed Dec. 22, 1949, with the patient under cyclopropane-ether anesthesia. When the pericardial sac was opened, poststenotic dilatation of the pulmonary artery was found. Even so, the dilated portion of the pulmonary artery was only 6 mm. in diameter. The infant's condition was precarious, and death seemed imminent. The valvulotome was quickly thrust through the wall of the visibly dilating right ventricle and guided into the pulmonary artery, where three radial incisions were hastily made. At the moment the stenosis was cut, the child's color improved promptly and the heart beat became regular.

The postoperative course was uneventful. When the patient was discharged, on the sixteenth postoperative day, there was no obvious cyanosis at rest but mild cyanosis was apparent on crying. There had been no change in the intensity or character of the preoperative cardiac murmur. Two months after operation the infant weighed 10 pounds 5 ounces (4,678 Gm.). He has been followed in the cardiac clinic for the past six months. His red blood cell count and hemoglobin value are now within normal limits and he is not cyanotic at rest; however, he becomes slightly cyanotic on crying. His general condition remains good. Roentgen examination of the chest shows considerable increase in vascularity of the lung fields.

Case 2.—L. B., a 13 month old white boy, weighing 16 pounds (7,257 Gm.), was admitted to the Children's Memorial Hospital in April 1950, with a history of cyanosis, irritability and recent failure to gain weight. A heart murmur was heard at birth, and at 3 days of age cyanosis first became apparent. Since the neonatal period cyanosis had been present constantly, had gradually increased in intensity and had been accentuated by exertion. Since 6 months of age he had failed to gain weight properly and his physical development had lagged behind that of his twin brother. In the month preceding his admission to the hospital he had had three typical and rather severe attacks of paroxysmal dyspnea.

Physical examination revealed a well nourished, fairly well developed infant with moderate cyanosis and mild clubbing of the fingers and toes, in addition to mild suffusion of the conjunctivas. The cardiac apex was in the fifth left interspace

just lateral to the nipple line. A grade 3 harsh blowing systolic murmur was present over the precordium, with maximal intensity in the third and fourth left interspaces near the sternum. A systolic thrill was palpable over this area. The second pulmonic sound was normal in intensity. The liver was ¾ inch (2 cm.) below the right costal margin in the nipple line, and the spleen was not felt.

Laboratory examination revealed a red blood cell count of 9,340,000 per cubic millimeter and a hemoglobin content of 17.0 Gm. per hundred cubic centimeters. A fluoroscopic examination showed definite diminution in the vascularity of the lung fields, with enlargement of the right auricular appendage and body of the right auricle. The right ventricle was moderately enlarged, and the pulmonary artery segment was rather prominent in the anteroposterior and right anterior oblique views (fig. 1). The electrocardiogram showed rather severe right heart strain with unusually tall and peaked P waves in all leads, especially in lead 2.

The diagnosis of pulmonary valvular stenosis with an interatrial septal defect was made.

An operation was performed April 6 with the patient under ether-cyclopropane anesthesia. The pulmonary artery at the point of emergence from the base of the heart was 6 mm. in diameter but promptly expanded to 15 mm. in diameter. The right ventricle was distinctly enlarged. The valvulotome was directed through the wall of the right ventricle into the pulmonary artery, where incisions were made in many directions. It was felt that since the stricture of the pulmonary artery itself was not remediable it was wise to relieve completely all obstruction within the lumen.

The postoperative course was uneventful. The child was comfortable out of oxygen and taking fluids well within thirty-six hours. He was discharged from the hospital on the eighteenth postoperative day. There was no obvious cyanosis at rest. A diastolic murmur over the pulmonic area was not heard, but all examiners were impressed with the fact that the preoperative systolic murmur had decreased in intensity following surgery. He was seen by one of us (W. J. P.) six weeks postoperatively and was getting along well, was no longer obviously cyanotic and was no longer suffering from attacks of paroxysmal dyspnea. His disposition was tremendously improved.

CASE 3.—E. H., a 10½ year old white boy, was admitted to the Children's Memorial Hospital in May 1950, with a history of increasing cyanosis and decreased exercise tolerance. Cyanosis and a heart murmur were first observed at 18 months of age. At the time of admission he was unable to walk more than four blocks and could run no more than fifty feet (15 meters).

Physical examination revealed a fairly well developed, fairly well nourished boy with moderate cyanosis and moderate clubbing of the fingers and toes. The cardiac apex was palpable in the fifth left interspace just lateral to the nipple line. A short systolic thrill was present with maximal intensity in the second left interspace. A grade 3 systolic murmur was audible over the precordium and was best heard in the first and second left interspaces. The pulmonic second sound was diminished in intensity. The liver was palpable at the right costal margin.

Routine roentgenographic and fluoroscopic examination revealed slightly decreased vascularity of the lung fields with a fairly prominent pulmonary artery segment in the anteroposterior and right anterior oblique views. The inflow and the outflow tracts of the right ventricle were distinctly enlarged, and the right auricle was slightly enlarged. A good pulmonary window was observed. The electrocardiogram showed an interventricular block probably involving the right bundle branch system. The P waves were rather tall and peaked in lead 2.

Angiocardiography demonstrated the passage of iodopyracet injection U. S. P. (diodrast®) from the superior vena cava into the right auricle and then crossing in a rather high concentration into the left auricle. A small main pulmonary artery was visualized, and the amount of dye passing into the pulmonary circulation appeared to be markedly decreased. There was no evidence of an overriding aorta.

Catheterization demonstrated normal relative values for the oxygen content in the venae cavae, the right atrium and the right ventricle. The pressure in the right atrium was not increased but was definitely increased in the right ventricle (138.5 systolic and 2.6 diastolic). The peripheral oxygen saturation was 65 volumes per cent. It was impossible to introduce the catheter into the pulmonary artery. The effective pulmonary flow was only one third of the systemic flow, suggesting that two thirds of the venous return was shunted from right to left and not passing through the lungs. The standard exercise test revealed a drop in the oxygen consumption per liters of ventilation from 24.2 to 22.4 cc.

The red blood cell count was 6,050,000 per cubic millimeter, and the hemoglobin was 16.5 Gm. per hundred cubic centimeters. The results of the remaining laboratory tests were within normal limits. Valvulotomy was advised.

The operation was done on May 25, 1950, with the patient under ether-cyclopropane anesthesia. The pulmonary artery was 13 mm. in diameter at the base of the heart and 20 mm. in diameter proximal to the point of bifurcation. Jets of blood could be felt squirting through the stenotic valve. Pressure in the pulmonary artery was 21 cm. of water. As soon as the valvulotome was thrust through the stenotic valve the intrapulmonary pressure began to rise and when incision was complete rose to 34 cm. of water. The increased pressure in the pulmonary artery was easily detectable with a palpating finger. The child's color improved instantly. The oxygen content of arterial blood as measured by oximeter promptly rose to 99 per cent saturation. Not more than 5 cc. of blood was lost during the intracardiac procedure.

The postoperative course was uneventful. The patient was awake and out of oxygen one hour after operation. Cyanosis was only suggestively present, and there was no change in the quality or character of the cardiac murmur. At the time of discharge from the hospital, sixteen days after operation, the arterial oxygen saturation, as determined by oximeter, was 93 per cent. Cyanosis was faintly present, and in addition to the preoperative systolic murmur there was now present a distinct grade 2 diastolic murmur beginning with the second sound and with maximal intensity in the second left interspace. The patient had already exercised himself along the corridors of the hospital and claimed that he no longer became tired or short of breath as he had before the operation. Six weeks after the operation violent exercise produced no visible cyanosis.

CASE 4.—R. S., a 2 month old white girl, was admitted to the hospital with the history of cyanosis from birth. She had been kept in oxygen intermittently for three weeks after birth. She was discharged home at the age of 4 weeks and in the intervening period had gotten along fairly well.

Physical examination revealed a fairly well developed white girl with mild cyanosis and no clubbing of the fingers or toes. The cardiac apex was in the fifth left interspace ½ inch (1 cm.) lateral to the nipple line. A precordial grade 3 systolic murmur was best heard in the third left interspace. The second pulmonic sound was quiet. The liver was ½ inch below the right costal margin, and the spleen was not felt.

Laboratory examination revealed a red blood cell count of 6,740,000 per cubic millimeter with a hemoglobin level of 18.4 Gm. per hundred cubic centimeters. Routine roentgenographic and fluoroscopic examination revealed diminished vascularity of the lung fields with moderate cardiac enlargement and a rather prominent pulmonary artery segment in the anteroposterior and right anterior oblique views. The inflow and outflow tracts of the right ventricle and the right auricular appendage were distinctly enlarged. There was no other chamber enlargement, and a good pulmonary window was present. The aortic arch lay to the left. The electrocardiogram revealed right heart strain with rather tall and peaked P waves, especially in lead 2.

A diagnosis of pulmonary valvular stenosis with an interatrial septal defect was made.

An operation was performed on May 19, 1950. Cyclopropane-ether anesthesia was administered. The valvulotome was inserted into the pulmonary artery and met with more resistance than in the previous 3 patients. A number of radial incisions were made. As the stenotic valve was being cut an increased thrill was palpable over the pulmonary artery. The child's

color improved immediately. Approximately 10 cc. of blood was lost during the intracardiac part of the operation.

The postoperative course was uneventful. Oral feedings were accepted within six hours after operation. The patient was discharged from the hospital on the twentieth postoperative day. No significant change in the intensity or character of the preoperative murmur was apparent at the time of discharge. No visible cyanosis was present, and the oxygen saturation as determined by oximetry was 92 per cent.

SUMMARY AND CONCLUSIONS

Four patients with pulmonary stenosis with intact ventricular septum have been treated surgically, with excellent results in all.

Transventricular incision of such pulmonary stenoses is a sound procedure.

The surgical technic of valvulotomy with a new and simple knife is described.

ACUTE PRIMARY KLEBSIELLA PNEUMONIA

MAURICE NATARO, M.D.
DAVID SHAPIRO, M.D.
and
ARMOND T. GORDON, M.D.
Louisville, Ky.

The management of lobar pneumonia due to Klebsiella pneumoniae (Friedländer's bacillus) continues to offer a real challenge to the clinician. As late as 1945 reports [1] indicated a mortality of 51 to 97 per cent. This is in contrast to the dramatic success in the treatment of the other bacterial pneumonias with the antibiotics. The incidence of lobar pneumonia caused by the gram-negative bacillus of the Friedländer group, Klebsiella pneumoniae, is variously reported as from 0.5 to 1.6 per cent of all cases of pneumonia; the disease may occur in all seasons. Although Hyde and Hyde [1a] were of the opinion that the sulfonamide drugs given early were of some benefit against the disease, their general conclusion was that the over-all value was questionable. Anderson [2] reported that K. pneumoniae is not susceptible to penicillin in vitro, and clinical experience substantiates this observation. In 1945 Heilman [3] reported in vitro and in vivo studies showing the effectiveness of streptomycin against infections due to K. pneumoniae. We can find only 10 cases [4] reported in the literature on the use of streptomycin in the treatment of acute primary Klebsiella pneumonia in the adult, but these showed a definite improvement over previously reported survival rates. A summary of the data on these cases is given in the accompanying table. In the latter part of 1948 reports [5] appeared that indicated the efficacy of aureomycin against K. pneumoniae experimentally. It was concluded that aureomycin, although it was slightly effective against infections due to K. pneumoniae, was less effective than either streptomycin or polymyxin. As recently as October 1949 Long [6] listed aureomycin as an antibiotic whose action on K. pneumoniae was unknown.

On the Medical Service of the Veterans Administration Hospital at Louisville, Ky., we have had the opportunity of treating 4 patients with acute primary lobar pneumonia due to K. pneumoniae with streptomycin. We have also used aureomycin in 1 case because we were anxious to use a less toxic drug than streptomycin and to verify the encouraging experimental results [5a] with aureomycin. As far as we are aware, there is at this time no published report on the use of aureomycin in acute primary Klebsiella pneumonia in man.

It is our purpose to report 4 cases of lobar pneumonia due to K. pneumoniae treated with streptomycin and 1 with aureomycin and to discuss the results of the use of these antibiotics.

REPORT OF CASES

Case 1.—H. R., a Negro aged 32, was admitted Jan. 21, 1948 with symptoms of an upper respiratory infection of one week's duration. He had awakened that morning with a severe pain in the left side of the chest that was aggravated by deep breathing. Later that day he noted rusty sputum. At times the sputum was pinkish or blood tinged. Chilly sensations were present.

Physical examination on admission revealed an acutely ill man with a temperature of 100.8 F., pulse rate 140 and respiratory rate 40. The pertinent physical observations were confined to the chest. There were diminished excursions of the chest and dulness to percussion over the midlung field on the left, with many moist rales and bronchial breathing over this area.

The red blood cell count on admission was 3,900,000, with 10 Gm. of hemoglobin. The total white blood cell count was 6,550, with a differential count of 84 segmented neutrophils and 16 lymphocytes. A Gram-stained smear of the sputum on the day after admission revealed many gram-negative encapsulated bacilli. The admission roentgenogram of the chest revealed a fairly dense, homogenous infiltration of the middle third of the left lung field, extending from the hilum to the periphery. There were no other significant abnormalities. Sputum cultures on January 22 and 23 and a blood culture on January 22 yielded a pure growth of K. pneumoniae.

Penicillin, 100,000 units intramuscularly every three hours, was given the patient immediately after admission. Treatment with streptomycin, 0.4 Gm. intramuscularly every four hours, was started on January 22, the day after admission. Supportive treatment included three 500 cc. transfusions of whole blood, intravenously given isotonic sodium chloride solution with 5 per cent dextrose and administration of oxygen. On this regimen the patient remained acutely ill, toxic, hallucinatory and disoriented. The temperature reached 105 and 106 F., rectally. A blood culture on January 27 did not grow any organisms. On this day the streptomycin dose was increased to 0.5 Gm. every four hours. The man showed little clinical improvement.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

From the Medical and Radiological Services of the Veterans Administration Hospital (Dr. Nataro, Assistant Chief in Medicine; Dr. Shapiro, Chief of Radiology, and Dr. Gordon, Senior Resident in Medicine) and from the Departments of Medicine and Radiology of the University of Louisville School of Medicine (Dr. Nataro, Associate in Medicine, and Dr. Shapiro, Assistant Professor of Radiology).

1. (*a*) Hyde, L., and Hyde, B.: Primary Friedländer Pneumonia, Am. J. M. Sc. **205**: 660-675 (May) 1943. (*b*) Solomon, S.: Primary Friedländer Pneumonia: Report of 32 cases, J. A. M. A. **108**: 937-947 (March 20) 1937.

2. Anderson, D. G.: Medical Progress: The Treatment of Infections with Penicillin, New England J. Med. **232**: 400-405 (April 5) 1945.

3. Heilman, F. R.: Streptomycin in the Treatment of Experimental Infections with Micro-Organisms of the Friedländer Group (Klebsiella), Proc. Staff Meet., Mayo Clin. **20**: 33-39 (Feb. 7) 1945.

4. (*a*) Bishop, C. A., and Rasmussen, R. F.: Klebsiella Pneumonia Treated with Streptomycin, J. A. M. A. **131**: 821-822 (July 6) 1946. (*b*) Learner, N., and Minnich, W. R.: Friedländer Pneumonia Treated with Streptomycin, Ann. Int. Med. **25**: 516-520 (Sept.) 1946. (*c*) Harris, H. W.; Murray, R.; Paine, T. F., and Finland, M.: Streptomycin Treatment of Pulmonary Infections, New England J. Med. **236**: 611-622 (April 24) 1947. (*d*) Vickery, C. E., and Gray, J.: Acute Friedländer's Bacillus Pneumonia Treated with Streptomycin, M. J. Australia **2**: 518-519 (Oct. 25) 1947. (*e*) Miller, B. W.; Orris, H. W., and Tans, H. H.: Friedländer's Pneumonia in Infancy, J. Pediat. **31**: 521-527 (Nov.) 1947. (*f*) Davis, J. P.; Cheek, K. M., and Harrell, S. T.: Friedländer Pneumonia with Bacteremia Successfully Treated with Streptomycin, North Carolina M. J. **8**: 767-769 (Dec.) 1947. (*g*) Robert, P., and Jutras, A.: Pneumonie à Friedländer guérie par la streptomycine, Union méd. du Canada **77**: 277-280 (March) 1948. (*h*) Keating, J. H., Jr.: Friedländer Bacillus Pneumonia Treated with Streptomycin, New York State J. Med. **48**: 1507-1508 (July 1) 1948. (*i*) Rosenthal, F. D.: Streptomycin in Friedländer Pneumonia, Lancet **2**: 743-744 (Oct. 22) 1949.

5. (*a*) Bliss, E. A., and Chandler, C. A.: In Vitro Studies of Aureomycin, Proc. Soc. Exper. Biol. & Med. **69**: 467-472 (Dec.) 1948. Chandler, C. A., and Bliss, E. A.: In Vitro Studies with Aureomycin, Ann. New York Acad. Sc. **51**: 221-227 (Nov. 30) 1948. (*b*) Bryer, M. S.; Schoenbach, E. B.; Bliss, E. A., and Chandler, C. A.: Treatment of Experimental Infections with Aureomycin, ibid. **51**: 254-266 (Nov. 30) 1948.

6. Long, P. H.; Chandler, C. A.; Bliss, E. A.; Bryer, M. S., and Schoenbach, E. B.: Use of Antibiotics, J. A. M. A **141**: 315-317 (Oct. 1) 1949.

The roentgenogram of the chest on January 30 revealed an extension of the pneumonic process, with complete obliteration of the markings over the whole left lung field. The white blood cell count was 32,400. In view of this, and because the sputum smears of January 29 and 30 revealed many gram-negative encapsulated bacilli, the streptomycin dosage was increased on January 29 to 1 Gm. every four hours. Sputum cultures and a blood culture on February 2 did not grow K. pneumoniae. Streptomycin therapy was discontinued on that date because the patient complained of nausea and headache, which were interpreted as manifestations of streptomycin toxicity. On February 4 he felt much improved, and the temperature began to fall by lysis. Thereafter he improved rapidly, and administration of penicillin was discontinued on February 10. A total dose of 42 Gm. of streptomycin and 8,000,000 units of penicillin had been given. The roentgenogram of the chest on February 18 revealed a clearing of the lower half of the left lung field. Throughout the upper half, which was still moderately opaque, were seen several areas of radiolucency. These were interpreted as probable areas of relative clearing and/or compensatory emphysema. The roentgenogram on March 3, 1948 revealed still further clearing in the upper lobe of the left lung without evidence of cavitation but with some peaking of the left diaphragm. The roentgenogram on May 3, 1948 revealed complete resolution of the process in the left lung except for a small radiodensity about 1.5 cm. in diameter, in the outer half of the second interspace. This was interpreted as most probably representing a localized patch of pleural thickening or fibrosis. The patient was discharged asymptomatic and afebrile on May 8. A follow-up roentgenogram of the chest on Aug. 10, 1948 revealed further regression of the small fibrotic patch in the left second interspace. At follow-up on Dec. 22, 1949 the roentgenogram revealed no essential changes as compared with that on Aug. 10, 1948.

Summary of Data on 10 Cases of Klebsiella Pneumonia Treated with Streptomycin

Case	Age and Sex	Days After Onset Before Streptomycin	Total Dosage	Course With or Without Cavities *	Result	Other Chemotherapy	Cultures: Blood	Cultures: Sputum	Lobes * Involv.	Roentgenograms on Discharge
Bishop and Rasmussen [48a]	59 F	14	1 Gm.	Rapid improvement	Well	Sulfadiazine and penicillin no effect	Throat positive		LLL	Complete resolution
Learner and Minnich [48b]	36 M	7	15.8 Gm.	Rapid improvement	Well	Penicillin no effect	—	+	LLL	Thickened interlobar fissure
Harris and others [48c]	54 M	6	15 Gm.	.....	Died	Penicillin and sulfadiazine no effect	—	+	RUL RML	.....
Harris and others [48c]	54 M	5	26 Gm.	Cavity in RML	Well	Penicillin for pneumococci	+	+	RML	Abscess gone in two months
Vickery and Gray [48d]	59 M	11	4.5 Gm.	No roentgenograms	Died	Penicillin and sulfadiazine	..	+	.....	.....
Miller, Orris and Taus [48e]	3 wk. M	12	6.7 Gm.	Cavities	? Well	Penicillin and sulfadiazine no effect	Nasal and sputum positive		RML LLL	Discharged 56 days after streptomycin therapy; still had cavities
Davis, Cheek and Harrell [48f]	16 M	6	31 Gm.	Improved slowly	Well	Penicillin and sulfadiazine no effect	+	+	RLL	Midpleural thickening at the right base
Robert and Jutras [48g]	22 F	9	40 Gm.	Improved slowly	Well	Penicillin no effect	..	+	Right lung	No residua
Keating [48h]	76 M	5	30.5 Gm.	Improved slowly; radiolucent areas	Well	Penicillin and sulfadiazine no effect	—	+	LLL	Fibrosis in LLL
Rosenthal [43]	54 M	40	50 Gm.	Cavities	Well	Penicillin and sulfathiazole no effect	..	+	LUL	No cavities; shift of mediastinum to left

* Letters RUL, RML, RLL, LUL and LLL denote right upper, middle and lower lobes and left upper and lower lobes, respectively.

CASE 2.—C. S., a white man aged 32, was admitted on April 6, 1948 in a semiconscious state. Ten days prior to admission pain developed in the right side of his chest, quickly followed by chills and fever. About four days prior to admission he had a cough productive of small amounts of rusty sputum. The day before admission he became delirious and exceptionally short of breath.

On admission the patient was semicomatose, had a temperature of 104 F., a pulse rate of 132 and a respiratory rate of 52. Physical examination revealed cyanosis, dulness to percussion over the upper lobe of the right lung and the right midlung field anteriorly with increased tactile fremitus and bronchial breathing but no rales over this area. The rest of the physical examination revealed essentially normal conditions.

The red blood cell count on admission was 4,390,000 with 13 Gm. of hemoglobin. The total white count was 7,100 with a differential of 78 segmented neutrophils, 3 stab cells, 18 lymphocytes and 1 eosinophil. A Gram-stained sputum smear on admission revealed many gram-negative encapsulated bacilli. This sputum eventually grew a pure culture of K. pneumoniae. A blood culture on April 12, before streptomycin therapy was started, failed to grow any organisms. A roentgenogram of the chest on admission showed massive involvement of the upper lobe of the right lung with a bulging of the horizontal fissure with the convexity downward.

The patient was placed in an oxygen tent and the administration of penicillin, 50,000 units intramuscularly every three hours, was started. There was no improvement, and the temperature ranged from 102 to 104 F. rectally. A roentgenogram of the chest on April 9 revealed slight clearing of the pneumonic process in the upper lobe of the right lung without evidence of cavitation. On April 12 a few relatively radiolucent areas were apparent in the upper lobe of the right lung, which were interpreted as areas of relative clearing and/or patchy areas of emphysema. There was no definite evidence of cavitation. In view of this, and because the patient had not shown clinical improvement after eight days of penicillin treatment, he was started on a regimen of streptomycin, 0.4 Gm. intramuscularly every four hours, on April 14. Penicillin therapy was continued. Within twenty-four hours after the first dose of streptomycin he displayed rapid clinical improvement, and the temperature began to fall by lysis. The temperature became normal on April 21 and both streptomycin and penicillin therapy were discontinued on April 22. The temperature remained normal thereafter. A total of 19.2 Gm. of streptomycin and 4,900,000 units of penicillin was given. A roentgenogram of the chest on April 20 showed almost complete clearing except for some peribronchial thickening in the upper lobe of the right lung. The final roentgenogram on May 5 revealed complete clearing of the pneumonic process in the upper lobe of the right lung. The patient was discharged asymptomatic on May 27, 1948.

CASE 3.—R. H., a white man aged 52, was admitted on June 19, 1948 complaining of inability to walk and of feeling "tired out." He also had a nonproductive cough. He was acutely ill with a temperature of 102 F., a pulse rate of 120 and a respiratory rate of 32. Physical examination revealed some impairment of respiratory excursions on the right. There

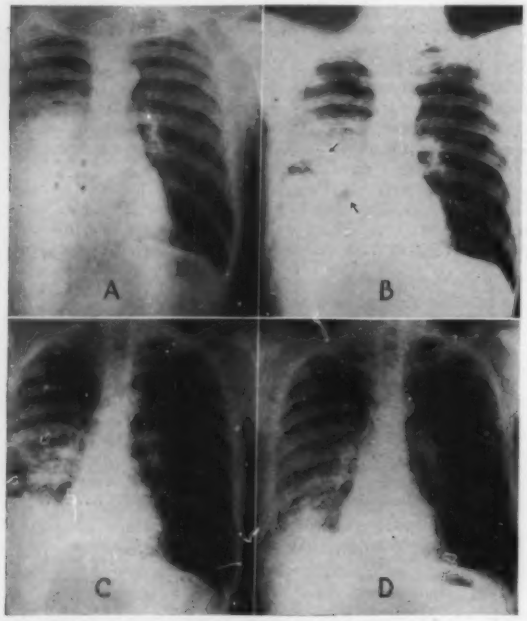

Fig. 1 (case 3).—Roentgenogram *A* shows dense, homogenous infiltration in the lower half of the right lung field. *B* and *C* show progressive clearing of the pneumonic process at the right lung base, with areas of relative radiolucency due to patchy areas of clearing and/or areas of emphysema. There is no definite evidence of cavitation. *D*, final roentgenogram, shows slight residual thickening of the pleura and increased markings at the base of the right lung.

was dulness to percussion over the middle lobe of the right lung and the lower third of the right lung fields with increased fremitus and many crepitant rales over this area. The liver was palpable 4 cm. below the costal margin in the right midclavicular line. In both legs there was 4 plus pitting edema extending up to the knees. The red blood cell count on admission was 3,950,000 with 11 Gm. of hemoglobin. The total white blood cell count was 16,750 with a differential of 80 segmented neutrophils, 7 stab cells, 11 lymphocytes and 2 basophils. The total protein was 4.10 Gm. per hundred cubic centimeters, with 2.28 Gm. of albumin and 1.82 Gm. of globulin. A Gram-stained sputum on admission revealed many gram-negative encapsulated bacilli. A culture of this sputum grew K. pneumoniae. Blood was not cultured. A roentgenogram of the chest on admission revealed a dense, homogenous infiltration of the lower half of the right lung field (fig. 1).

Immediately after admission he was put in an oxygen tent and given penicillin, 100,000 units intramuscularly, every three hours. He did not improve. The temperature reached 103.6 F. rectally, and he became more confused. A roentgenogram of the chest on June 29 showed slight clearing of the pneumonic process at the base of the right lung, and multiple areas of relative radiolucency were now observed in the same region. Sputum smears on June 24 and 25 revealed many gram-negative encapsulated bacilli. On June 28 he began to bring up large amounts of sputum variously described as prune-juice, brown or plum colored. In view of the foregoing observations, treatment with streptomycin, 0.4 Gm. intramuscularly every four hours, was started on June 29. Penicillin therapy was continued. He began to improve clinically within forty-eight hours, although he still had a low grade fever. A roentgenogram on July 7 revealed slight further clearing of the pneumonic process. There were still areas of relative radiolucency at the base of the right lung. These were interpreted as patchy areas of clearing and/or areas of emphysema. There was still no definite evidence of cavitation. Because of the continued fever, streptomycin dosage was increased to 1 Gm. every four hours on July 6. The amount of sputum became normal, and the patient became asymptomatic. Numerous sputum cultures after admission grew K. pneumoniae. Streptomycin was discontinued on July 16 and penicillin on August 11. Numerous sputum cultures after August 6 failed to grow the organism. He remained asymptomatic and afebrile. A roentgenogram of the chest and fluoroscopy on August 24 revealed some further clearing in the lower half of the right lung field, but there were now a small amount of fluid and pleural thickening at the right base. Thoracentesis was performed on August 25 and about 1 cc. of thick mucoid material was withdrawn. This was cultured and grew K. pneumoniae. A roentgenogram on August 31 revealed further clearing, but there remained patchy areas of pleural thickening and slight peribronchial haziness at the right base. The horizontal fissure on the right was also thickened. The roentgenogram of the chest on Nov. 13, 1948 again showed slight residual thickening of the pleura and increased markings at the right lung base (fig. 1). The patient received a total of 16.8 Gm. of streptomycin and 20,800,000 units of penicillin. He was discharged asymptomatic and afebrile on Nov. 15, 1948.

CASE 4.—J. O., a Negro aged 44, was admitted on Nov. 14, 1948 in a semicomatose state. Two days prior to admission he had a chill, then fever and pain in the left side of the chest; later he noted a cough that was productive of moderate amounts of tenacious bloody sputum. The day prior to admission he experienced severe shortness of breath. On admission the temperature was 100.2 F., the pulse rate 104 and the respiratory rate 32. The pertinent physical observations were confined to the chest. The respirations were shallow and accompanied with an expiratory grunt. There was dulness to percussion over the left lower part of the chest posteriorly with increased tactile fremitus and many sibilant rales over this area. Many moist rales were heard over the entire left side of the chest.

The red blood cell count was 4,400,000 with 13 Gm. of hemoglobin. The total white blood cell count was 3,500. The admission sputum revealed many gram-negative encapsulated bacilli. This sputum grew K. pneumoniae. The roentgeno-

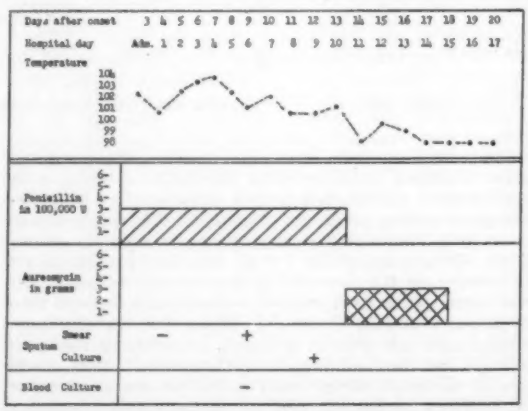
Days after onset 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Hospital day Adm. 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
Temperature
104
103
102
101
100
99
98
Penicillin in 100,000 U
Aureomycin in grams
Sputum Smear
Culture
Blood Culture

Fig. 2 (case 5).—Correlation of clinical and laboratory data with penicillin and aureomycin therapy.

gram of the chest revealed a homogenous and a fairly dense infiltration in the lower half of the left lung field. Incidental observations were old healed fractures with partial resection of the eighth and ninth ribs on the right side and old healed fractures of the sixth, seventh and eighth ribs on the left.

Immediately after admission the patient was put in an oxygen tent and started on a regimen of 100,000 units of penicillin intramuscularly every three hours. There was no

response to this therapy over a period of twenty-four hours. Because another sputum smear on November 16 had shown many gram-negative encapsulated bacilli, he was given streptomycin, 0.4 Gm. every four hours intramuscularly, and the penicillin dosage was increased to 100,000 units every two hours. He received several transfusions of whole blood and plasma. A white blood cell count on November 16 was 2,450. He did not respond to therapy and expired on the evening of Nov. 16, 1948. A blood culture and a lung aspiration on the day the patient expired later grew K. pneumoniae. He received a total of 1.2 Gm. of streptomycin and 2,000,000 units of penicillin.

CASE 5.—A. P., a Negro aged 28, was admitted on Aug. 18, 1949, stating that three days prior to admission he noted a sharp pain in the left side of his chest which was aggravated by deep breathing. This was soon followed by chills, fever and a nonproductive cough. On admission he was acutely ill. The positive physical observations were confined to the respiratory system. There was dulness to percussion over the left lung base posteriorly, with inspiratory crepitant rales over the same area.

The admission roentgenogram revealed infiltration of the medial half of the left pulmonary base and a slight elevation of the dome of the diaphragm on the left. The red blood cell count on admission was 4,520,000 with 13.5 Gm. of hemoglobin. The total white blood cell count was 24,100. He was immediately given penicillin, 100,000 units intramuscularly every eight hours, but showed no improvement. A roentgenogram of the chest on August 22 revealed spread of the pneumonic process with massive involvement of the whole lower lobe of the left lung and bulging of the interlobar fissure. A sputum smear on August 24 revealed gram-negative bacilli, and this later grew K. pneumoniae. A roentgenogram of the chest on August 29 did not show any change.

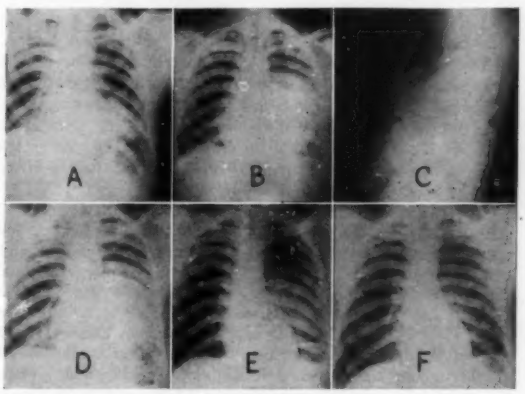

Fig. 3 (case 5).—Admission roentgenogram (*A*) shows infiltration, left lung base. *B* and *C* show spread of disease with involvement of whole left lower lobe and bulging of the interlobar fissure. *D* shows essentially no change from the previous roentgenogram; aureomycin therapy was started on this date. *E* shows moderate clearing one week later. In *F*, the final roentgenogram, both lung fields are clear.

The patient was ill and semicomatose when treatment with aureomycin hydrochloride was started. He was given 1 Gm. by mouth every six hours on August 29, when penicillin therapy was stopped. He began to improve rapidly from a clinical point of view within twenty-four hours, and his temperature became normal at the end of forty-eight hours and remained so thereafter. Administration of aureomycin was discontinued (fig. 2) on September 3. He received a total of 20 Gm. of aureomycin over the five day period; he had received a total of 3,300,000 units of penicillin prior to the aureomycin. A roentgenogram of the chest on September 6 showed moderate but definite clearing of the infiltration in the lower lobe of the left lung without evidence of cavitation. A roentgenogram on Oct. 20, 1949 showed both lung fields to be completely clear with no residual of the previous infection evident (fig. 3).

COMMENT

It is generally acknowledged that the sulfonamide drugs and penicillin are relatively ineffectual in the treatment of acute primary Klebsiella pneumonia. In our series the patients did not show a significant response to penicillin. In 3 cases there was increased toxicity and actual spread of the lesion as evidenced by roentgen examinations of the patient while receiving adequate penicillin dosage.

Since the advent of streptomycin therapy the results against K. pneumoniae have been encouraging. Heretofore it was estimated [1b] that approximately one sixth of the patients recovered, about one third progressed to the chronic phase of the disease (fibrosis, bronchiectasis and/or cavitation) and about one half died. Our 4 cases with streptomycin therapy and the 10 cases reviewed from the literature, also with streptomycin therapy, do show a decrease in the number of patients whose disease progresses into the chronic phase. There were only 2 patients in this total series who displayed roentgenologic evidence of cavitation or severe fibrosis at the time of discharge or at follow-up.

Streptomycin has shown itself to be a potent antibiotic in the management of acute primary Klebsiella-caused pneumonia. However, because of the known toxic effects of streptomycin and because Chandler and Bliss had shown that aureomycin was promising in the treatment of experimental infections with bacilli of the Friedländer group, we decided to try it in 1 case. The patient (case 5) was becoming clinically worse, and roentgen examination revealed evidence of advanced spread of the disease process in spite of penicillin therapy. On the thirteenth day after the onset aureomycin therapy was started, and the results were dramatic. Within twenty-four hours there was decided clinical improvement of the patient, and by the end of the second twenty-four hours the temperature had dropped to normal. Roentgen examination of the chest (fig. 2) one week after administration of aureomycin was started showed more rapid improvement than was usual after treatment with streptomycin for the same time interval.

Although the over-all mortality rate of the whole series was 20 per cent, 2 of the 3 patients who died did so less than twenty-four hours after the start of streptomycin therapy and cannot be considered to have had an adequate trial on the drug.

Regardless of how long after the onset of the disease treatment with streptomycin was started, the drug was found to be highly effective in either curing the infection or greatly reducing the incidence of the chronic phase. On the basis of our experience, the recommended dosage schedule is 0.4 Gm. of streptomycin every four hours for a seven to ten day period.

We believe that the radiologist can be of definite aid in arriving at an early diagnosis, principally by having a high index of suspicion in all cases in which there is massive, dense and usually homogenous lobar consolidation, particularly when there is bulging of the fissure. We do not believe that the degree of radiopacification of the involved lung is of any diagnostic significance, as similar densities may be found in other forms of pneumonia with a comparable extent of disease.

The tendency for early development of abscesses and subsequent cavitation has been stressed since the reports of Apelt [7] and Kornblum.[8] However, we should caution

7. Apelt, F.: Ueber die durch den Bazillus Pneumoniae Friedlaender hervorgerufene Pneumonie, München. med. Wchnschr. **55**: 833-837, 1908.
8. Kornblum, K.: Roentgen-Ray Diagnosis of Pulmonary Infections with the Friedländer Bacillus, Am. J. Roentgenol. **19**: 513-521 (June) 1928.

against the reporting of circular areas of partial clearing with resultant relative radiolucency and/or temporary areas of obstructive or compensatory emphysema as cavities (fig. 1). In this regard there are probably frequent errors of commission because of anticipation of the well recognized and not infrequent complication of cavity formation.

Although our series is relatively small, the fact that definite evidence of cavity formation was not apparent in any instance suggests that early treatment with streptomycin or aureomycin will reduce the incidence of cavity formation and chronic fibrosis.

SUMMARY

1. A review of the pertinent literature on the treatment with streptomycin of acute primary pneumonia caused by Friedländer's bacillus, Klebsiella pneumoniae, has been presented and 4 additional cases have been reported.

2. Penicillin and the sulfonamide drugs have been found to be ineffective against this condition.

3. Streptomycin is an effective agent in the treatment of acute primary Klebsiella pneumonia.

4. Aureomycin hydrochloride was used in 1 case and the results were dramatic, suggesting that further clinical trial and evaluation are indicated.

5. Mortality and morbidity of the disease seem to be significantly diminished when streptomycin and aureomycin are used.

6. Although the radiologic observations are not pathognomonic, in many cases they may be highly suggestive of the correct diagnosis and may be a factor leading to early discovery of K. pneumoniae in the sputum or blood.

PULMONARY METASTATIC LESION SUCCESSFULLY TREATED WITH RADIOACTIVE IODINE

Report of a Case of Pulmonary Metastasis from a Papillary Adenocarcinoma of the Thyroid

A. STONE FREEDBERG, M.D.
ALVIN L. URELES, M.D.
MARK F. LESSES, M.D.
and
SAMUEL L. GARGILL, M.D.
Boston

In 1942 Keston, Ball, Frantz and Palmer [1] reported significant uptake and storage of radioactive iodine (I^{131}) in a metastasis in the femur from a "malignant adenoma" of the thyroid. At necropsy only one of many metastatic lesions examined contained a significant concentration of I^{130}. Histologically this metastasis resembled differentiated thyroid tissue. Other histologically undifferentiated metastases showed no uptake. These authors suggested that effective therapeutic internal irradiation might be achieved in well differentiated thyroid tumors and metastases.

In 1946 Seidlin, Marinelli and Oshry [2] recorded the successful treatment with I^{130} and I^{131} of a patient with adenocarcinoma of the thyroid, removed twenty-one years previously, with subsequent widespread metastases to the lungs, femur, ribs, vertebrae, ilium and skull. The patient presented clinical and laboratory evidence of hyperthyroidism, and the metastatic lesions were demonstrably avid for radioactive iodine. Subsequent to radioactive iodine therapy there was definite improvement reflected by disappearance of pain, increase in weight and the development of hypothyroidism. Roentgenograms pointed to "an arrest if not a regression" of the metastases. Recent papers [3] describe the maintenance of improvement in this patient over a period of five years.

Several groups have since reported their experience with the treatment of thyroid carcinoma with I^{131} ; [4] approximately one third of the total number of 30 reported patients have shown improvement consequent to I^{131} therapy. This paper presents in detail the history of a 14 year old boy with carcinoma of the thyroid gland and a solitary pulmonary metastasis treated with I^{131}. The pulmonary lesion disappeared two months after therapy was initiated, and in the subsequent twelve months there has been no evidence of recurrence.

REPORT OF CASE

S. S., a 12 year old boy, entered the Beth Israel Hospital in December 1946 because of a painless mass in the neck of three months' duration. There had been no dysphagia, dyspnea or hoarseness. There had been no symptoms of thyrotoxicosis.

At the age of 11 weeks the patient had been seen at the pediatric clinic with signs of an enlarged thymus. After four roentgen treatments, the thymic shadow was no longer visualized on roentgen examination.

On physical examination the pulse rate was 80 and the blood pressure was 110 systolic and 80 diastolic. There was a firm, walnut-sized mass, which moved on swallowing, in the right lobe of the thyroid. The other results of the physical examination were not remarkable. The hemoglobin was 12.3 Gm. (Sahli), and the urine was normal.

On Dec. 23 right hemithyroidectomy and an excision of the thyroid isthmus was performed. At operation the mass was discrete, plum sized, firm and slightly granular and replaced the right lobe. It was not adherent to the overlying muscles but was fixed to the trachea.

Pathologic Description.—The specimen consisted of 17 Gm. of multilobular irregular tissue. The external surface was covered by a thin fibrous capsule except at the plane of resection. The cut surface was composed of homogeneous light yellow-tan, firm tissue divided into three lobes. The largest lobe measured 2.0 cm. in average diameter, and the smallest lobe averaged 0.6 cm. in diameter. Attached to the specimen was a small amount of softer tissue 1.0 cm. in average diameter whose cut surface was beefy red and resembled normal thyroid tissue.

On microscopic examination the tumor tissue consisted of papillary folds covered by layers of tall columnar epithelium, the nuclei of which were basally placed and exhibited frequent mitotic figures. The papillary folds were irregular and anastomosing and formed irregular, markedly tortuous channels, some of which were filled with colloid material. Through the center of each papillary process was a simple narrow stalk com-

From the Medical Research Department, Yamins Research Laboratory, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School, Boston.

This work was carried out under a contract between the Office of Naval Research, Atomic Energy Commission and the President and Fellows of Harvard College. Support was also obtained from the Anna Wasserman Lowenberg Fund.

1. Keston, A. S.; Ball, R. P.; Frantz, V. K., and Palmer, W. W.: The Storage of Radioactive Iodine in the Metastases from Thyroid Carcinoma, Science **95**: 362, 1942.

2. Seidlin, S. M.; Marinelli, L. D., and Oshry, E.: The Therapeutic Effect of Radioactive Iodine on Functioning Metastases of Thyroid Adenocarcinoma, J. A. M. A. **132**: 838 (Dec. 7) 1946.

3. (*a*) Seidlin, S. M.; Oshry, E., and Yalow, A.: Twelve Cases of Metastatic Carcinoma of the Thyroid Studied with Radioactive Iodine, abstracted, J. Clin. Endocrinol. **7**: 467, 1947. (*b*) Seidlin, S. M.; Rossman, I.; Oshry, E., and Siegel, E.: Radioiodine Therapy of Metastases from Carcinoma of the Thyroid: A Six Year Progress Report, J. Clin. Endocrinol. **9**: 1122, 1949.

4. (*a*) Marinelli, L. D.; Trunnell, J. B.; Hill, R. F., and Foote, F. W.: Factors Involved in the Experimental Treatment of Metastatic Thyroid Carcinoma with Radioactive Iodine I^{131}, Radiology **51**: 553, 1948. (*b*) Trunnell, J. B., and others: The Treatment of Metastatic Thyroid Cancer with Radioactive Iodine: Credits and Debits, J. Clin. Endocrinol. **9**: 1138, 1949. (*c*) Rawson, R. W.; Marinelli, L. D.; Skanse, B.; Trunnell, J., and Fluharty, R.: The Effect of Total Thyroidectomy on the Function of Metastatic Thyroid Cancer, J. Clin. Endocrinol. **8**: 826, 1948. (*d*) Salter, W. T., and MacAllister, W. J.: Iodine: Radioactive and Stable in Normal and Cancerous Tissues, Tr. A. Am. Physicians **61**: 210, 1948. (*e*) Frantz, V. K.; Quinby, E. H., and Evans, C.: Radioactive Iodine Studies of Functional Thyroid Cancer, Radiology **51**: 532, 1948.

posed of compressed strands of collagen fibers. In other portions of the tumor there were follicles, lined by tall columnar epithelium, containing scanty colloid material (fig. 1). Most of the tumor was enclosed by a fibrous capsule of varying thickness. In several areas tumor cells had invaded the capsule, and in other areas portions of the tumor forming follicles invaded the surrounding normal thyroid (fig. 1). The histologic diagnosis was papillary adenocarcinoma. Four slides were submitted to the pathology departments of two other hospitals; the diagnosis was papillary cystadenocarcinoma of the thyroid gland.

Clinical Course.—The patient made an uneventful recovery and approximately two weeks later reported to the tumor clinic for roentgen therapy. The hemoglobin was 11.8 Gm., red blood cell count 4,100,000; white cell blood count 6,800; the differential

TABLE 1.—*Radioactivity* (I^{131}) *Measurements Over the Thorax (Patient S. S.)*

Site	Side	Time for 4,096 Counts, Min.
Spine of scapula	Left	1.10
	Right	0.92
Angle of scapula	Left	1.33
	Right	0.34
Anterior fourth interspace	Left	0.85
	Right	0.96
Anterior sixth interspace	Left	1.1
	Right	1.0

count and thrombocytes (platelets) were normal. On roentgen examination there were no localized pulmonary consolidations or metastatic or destructive bone lesions. During the next four weeks, the patient received 3,850 r to the anterior thyroid region. The factors were 200 kilovolts, 0.5 mm. of copper and 1 mm. of aluminum, at 50 cm. distance through a 10×10 cm. field.[5] Pharyngitis, hoarseness and epidermitis followed and subsided. In the succeeding nine months he was asymptomatic. There was no evidence of local thyroid recurrence, and on roentgen examination the lung fields were clear. The basal metabolic rate was + 10 per cent and the pulse rate, 73.

In December 1947, one year after operation, the patient noted pain in the right side of the chest. Physical examination showed no abnormalities. A roentgenogram showed a rounded area of increased density less than 1.0 cm. in diameter in the right midlung field (fig. 2*A*). The patient returned to the clinic in

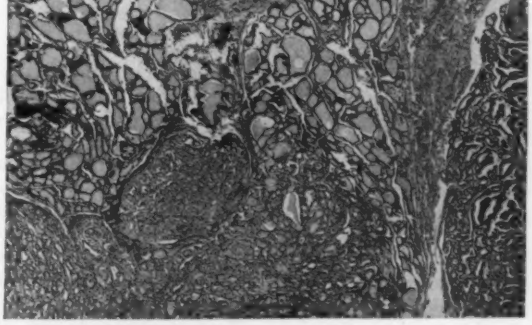

Fig. 1.—Histologic section of thyroid gland showing encapsulated papillary carcinoma with adenocarcinoma invading normal thyroid tissue (× 180). All illustrations refer to patient S. S.

March 1947, three months after thyroidectomy, at which time he was asymptomatic. A repeat roentgenogram of the chest showed no change in the pulmonary lesion. In the ensuing months repeated roentgenologic examinations showed slow progressive increase in the size of the pulmonary lesion. In December 1948 it was 1.5 cm. in diameter (fig. 2*B*), an increase of approximately 1.0 cm. during the preceding twenty months.

Tracer Studies.—On Nov. 20, 1948 a 1.8 millicurie[6] tracer dose of I^{131}, carrier free, was administered, and in the following seventy-two hours 79 per cent[7] was excreted in the urine (fig. 3). The uptake in the thyroid region as measured with a single end-window Geiger-Mueller tube was in the euthyroid range. Radioactivity measurements[8] over the surface of the

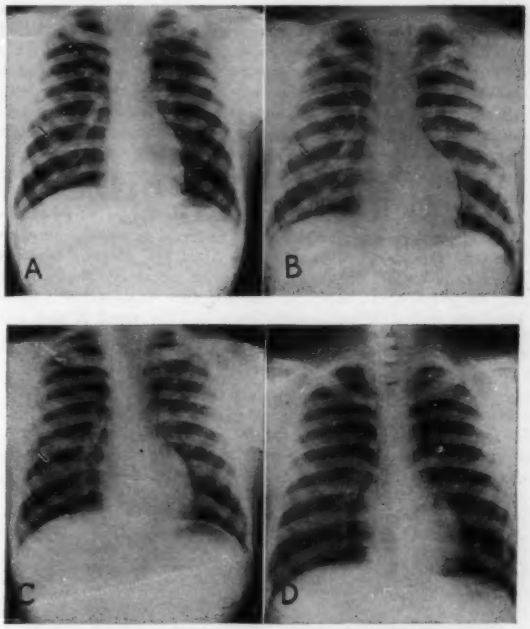

Fig. 2.—Chest roentgenograms *A*, taken Dec. 23, 1947, one year postoperatively, showing a rounded area of increased density, less than 1 cm. in diameter in the right midlung field. *B*, taken Dec. 27, 1948, two years postoperatively, and twelve days before I^{131} therapy, the lesion in the right midlung field now measures 1.5 cm. in diameter. *C*, taken Jan. 28, 1949, twenty days after the oral administration of 78 millicuries of I^{131}. The lesion has decreased in size and the shadow has lost its consolidated appearance. *D*, taken May 6, 1949, four months after the first therapeutic dose of I^{131} and three and a half months after fig. 2*C*. Subsequent roentgenograms are similar.

body were made, and a discrete area of radioactivity was noted at the inferior angle of the right scapula. In this region, corresponding to the lesion noted on roentgen examination, counts per minute were four times those obtained in surrounding areas or in a comparable area over the other lung (table 1).

Second Hospital Admission.—The patient was admitted Dec. 27, 1948 for I^{131} therapy. There were no masses palpable in the right side of the neck, and the left thyroid lobe was not palpable. The trachea was in the midline. The lungs were normal. Other results of the physical examination were normal.

Laboratory Data.—Results of urine and stool examinations were normal. The hemoglobin was 14.5 Gm., the red blood cell count 5,300,000 per cubic millimeter. The white blood cell count ranged from 6,000 to 9,500 per cubic millimeter; the differential count was normal. The corrected sedimentation rate was 0.25 mm. per minute (Rourke-Ernstene method—normal 0.08 to 0.35 mm. per minute). The serum cholesterol averaged 320 mg. per hundred cubic centimeters.[9] Four consecutive basal metabolism measurements averaged — 13 per cent (range — 6 to — 16). On roentgen examination the pulmonary metastasis

5. Dr. Bernard A. Levine supplied the roentgen therapy data.

6. The millicurie utilized in this study conforms to that of the United States Bureau of Standards.

7. Freedberg, A. S.; Buka, R., and McManus, M. J.: Comparative Value and Accuracy of Measurements of Urinary I^{131} by Beta and by Gamma Ray Counting, J. Clin. Endocrinol. **9**: 841, 1949.

8. Freedberg, A. S.; Ureles, A. L.; Gargill, S. L., and Lesses, M. F.: The Treatment of Thyroid Carcinoma with I^{131}, to be published.

9. Myers, J. C., and Wardell, E. L.: The Colorimetric Estimation of Cholesterol in Blood with a Note on the Estimation of Coprosterol in Feces, J. Biol. Chem. **36**: 147, 1918. Ling, S. M.: The Determination of Cholesterol in Small Amounts of Blood, J. Biol. Chem. **76**: 361, 1928.

was located in the right lower lobe close to the posterior chest wall; in the lateral view it was superimposed on the ninth vertebra. There was no evidence of metastatic malignancy in the long bones of the upper and lower extremities, in the thoracic or lumbar spine or in the pelvis.

Treatment.—On Jan. 8, 1949, 78 millicuries, carrier free, of I^{131} was administered orally. In the subsequent six days, 77 per cent was excreted in the urine (fig. 3); 70 per cent had been excreted in the first forty-eight hours. During this period the patient was in a separate room. The uptake in the thyroid gland area measured by the four tube method [10] was 20 per cent in the euthyroid range. During the first forty-eight hours after treatment with I^{131}, anorexia and nausea developed, followed by pain, localized warmth and tenderness over the left thyroid lobe. The pain and tenderness subsided without treatment during the following four days. Measurements over the anterior and posterior surface of the thorax five days after administration of I^{131} showed a localized area of increased radioactivity over the right midscapula. External measurements with the four tube method, twenty days after I^{131} therapy, showed more radioactivity in the region of the metastasis than in the thyroid gland area (table 2). On roentgen examination at this time, the metastatic pulmonary lesion had decreased in size, and the shadow appeared to be resolving (fig. 2*C*).

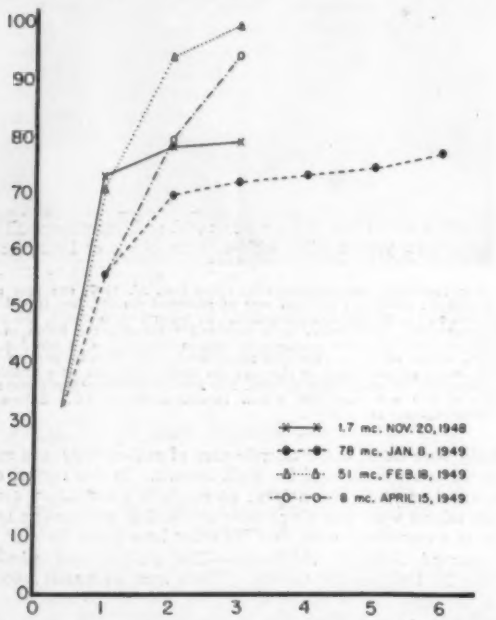

Fig. 3.—The urinary excretion of I^{131} following the administration of therapeutic doses of I^{131}. The curve -Δ-Δ- was obtained six weeks after the first therapeutic dose at a time when the patient was first beginning to show evidences of mild hypothyroidism. The curve O-O was obtained during marked myxedema. The twenty-four hour urinary excretion is not shown in this curve. The point coincided with the twenty-four hour urinary I^{131} excretion following the 78 millicurie dose. The vertical column of figures on the left indicates the percentage of urine excretion (cumulative) and the horizontal row of figures indicates the number of days.

Six weeks after the first dose, 51 millicuries of I^{131} was administered and 99 per cent excreted in the urine in the following seventy-two hours (fig. 3). At the end of twenty-four hours the uptake in the thyroid gland region [10] was 6 per cent and at seventy-two hours, 0.3 per cent. There were no extrathyroid sources of radioactivity, and no increased radioactivity could be demonstrated over the right lung field. On Feb. 23, 1949, seven weeks after the first dose of I^{131}, the basal metabolic rate was —27 per cent, the serum cholesterol 439 mg. per hundred cubic centimeters. During the previous week, the patient had noted sluggishness and sleepiness. His voice was hoarse, his face puffy and pale, and the skin cool and smooth. On March 11, two months after the first therapeutic dose, the basal metabolic rate was —37 per cent. He complained of fatigue, poor memory, clumsiness and stiffness and pain in the knees. A roentgenologic examination showed the lung fields entirely clear, and there was no evidence of metastatic malignancy in the bones or skull. The administration of *d*-amphetamine sulfate (5 to 10 mg. of dexedrine®) daily resulted in increased alertness. The signs of myxedema persisted, however, and the basal metabolic rate was —30 per cent and the cholesterol 614 mg. per hundred cubic centimeters. On April 15, 1949, three and a half months after the first therapeutic dose of I^{131}, a third dose of 8 millicuries was administered orally. During the following seventy-two hours, 99 per cent was excreted in the urine (fig. 3). There was no uptake in the thyroid gland area and no localization or concentration of the radioactivity in the body. The administration of desiccated thyroid, 15 mg. daily, was begun one month later, or two and a half months after the development of myxedema.

TABLE 2.—*Radioactivity* (I^{131}) *Measurements Twenty Days After an Oral Dose of 78 Millicuries (Patient S. S.)*

Site	Time (Minutes) for 4,096 Counts/Min.	Background Counts/Min.	Net Counts/Min.	Calculated Uptake of Dose (%)
Thyroid gland area.....	1.40	300	2,620	0.32
Region of pulmonary metastasis	0.72	300	5,390	0.65

Desiccated thyroid was increased to 60 mg. daily with rapid subsidence of the symptoms and signs of myxedema. In August 1949, seven months after the first therapeutic dose of I^{131}, the patient felt entirely well and had resumed all his normal activities, including baseball and swimming. When seen in January 1950, he weighed 132 pounds, (59 Kg.) a 14 pound (6.4 Kg.) gain in weight, and felt entirely well. His school work is of honor caliber. During the previous two months sexual maturity had occurred. There was no palpable thyroid tissue in the neck. The skin was normal. Axillary and pubic hair were present. The external genitalia were normal. The basal metabolic rate was —17 per cent, the serum cholesterol 238 mg. per hundred cubic centimeters. A complete blood count was normal, and roentgenograms of the lung (fig. 2*D*) and long bones showed normal conditions. The dose of desiccated thyroid was increased to 90 mg. daily.

COMMENT

A striking result was achieved with radioactive iodine in this patient. Unlike the original case reported by Seidlin, Marinelli and Oshry,[2] this patient had no clinical or laboratory evidence of hyperthyroidism. After the first dose of 78 millicuries of I^{131}, there was complete disappearance of the metastatic pulmonary lesion, and on subsequent therapeutic or tracer doses of I^{131} there was no evidence of localization or concentration of I^{131} in the area of the metastasis. The first therapeutic dose also resulted in complete destruction of the functioning thyroid tissue in the neck, as evidenced by the development of myxedema and the absence of I^{131} uptake after its administration. The destruction of the metastatic lesion concomitantly with the destruction of thyroid tissue in the neck is unusual. Only 1 of 25 patients reported by Trunnell and his associates [4b] showed metastatic tumor tissue which concentrated enough radioactive iodine to justify administering this isotope in therapeutic doses before subjecting the patient to surgical removal of the thyroid. This emphasizes the importance of the tracer study in this patient in which

10. Freedberg, A. S.; Ureles, A., and VanDilla, M.: (*a*) Quantitative Measurement by External Counting of the I^{131} Content of the Thyroid Gland in Man, Federation Proc. **8**:1, 1949; (*b*) Studies with a New Method for Quantitative Measurement of I^{131} Content of the Thyroid Gland in Man, J. Clin. Investigation **28**:4, 1949.

evidence of uptake was demonstrated in the metastasis as well as in the area of the thyroid gland.

The exact nature of the metastatic lesion in this patient is not known; the location and size of the lesion precluded biopsy. The pathologic report on the surgically removed right lobe of the thyroid gland was papillary adenocarcinoma, and the pathologist noted that the tumor appeared to be of low grade malignancy. The age of the patient and clinical course are consistent with these observations. The increased avidity of the metastatic lesion for I^{131} is consistent with the view that the tumor was differentiated.[11]

Seidlin and others [12] and Rawson and others [4b, c] have shown that increased uptake in metastatic lesions followed the development of myxedema. Accordingly, we allowed complete myxedema to develop and persist in this patient for two and a half months before desiccated thyroid was administered. A longer period was not considered practical because of the severe discomfort associated with myxedema. No evidence was obtained during this time of new metastatic lesions. The administration of desiccated thyroid resulted in prompt relief of the symptoms of myxedema.

The adverse effects of I^{131} in this patient were mild and required no specific therapy. Careful examination of the urine and blood in the period immediately following the therapeutic doses showed no change, and results of follow-up studies during the subsequent twelve months were completely normal. The normal sexual development in this patient is consistent with other observations of the low uptake and concentration of I^{131} in the gonads.[13]

SUMMARY AND CONCLUSIONS

A metastatic lesion was demonstrated in the right lung of a 14 year old boy one year following a right hemithyroidectomy for papillary adenocarcinoma of the thyroid gland. The uptake of I^{131} in the area of the metastasis following a tracer dose was four times that of an uninvolved control area. Two months after the administration of 78 millicuries of I^{131} the lung lesion had resolved and there was no observable concentration of radioactive iodine over the thyroid area or over the previous metastatic area. Thyrotoxicosis was not observed, and there were no toxic effects on the kidneys or blood. Two months after the first therapeutic dose symptoms, signs and laboratory evidence of myxedema were observed. After two additional doses of radioactive iodine (a total of 137 millicuries), there was no evidence of localization or concentration of radioactive iodine within the body. At the present time, twelve months after the first therapeutic dose of I^{131} and seven months after the commencement of desiccated thyroid therapy, he is entirely well. The basal metabolic rate is —17 per cent and the serum cholesterol 238 mg. per hundred cubic centimeters. There is no evidence of metastatic recurrence in the neck, lungs, long bones, skull or pelvis.

11. (*a*) Keston, Ball, Frantz, and Palmer.[1] (*b*) Frantz, Quinby, and Evans.[1c] (*c*) Leiter, L.; Seidlin, S. M.; Marinelli, L. D., and Bauman, E. J.: Adrenocarcinoma of the Thyroid with Hyperthyroidism and Functional Metastases: I. Studies with Thiouracil and Radioactive Iodine, J. Clin. Endocrinol. **6**: 247, 1946. (*d*) MacArthur, J. W., and Cope, O.: The Functional Capacity of Thyroid Tumors as Judged by Their Radioactive Iodine Uptake, J. Clin. Investigation **25**: 929, 1946. (*e*) Marinelli, L. D.; Foote, F. W.; Hill, R., and Hocker, A.: The Retention of Radioactive Iodine in Thyroid Cancer, Am. J. Roentgenol. **58**: 17, 1947. (*f*) Rawson, R. W.; MacArthur, J. W.; Dobyns, B. M., and Fluharty, R. G.: The Functional Activity of Thyroid Tumors Benign and Malignant, as Gauged by Their Collection of Radioactive Iodine, West. J. Surg. **56**: 82, 1948. (*g*) Fitzgerald, P.: The Histologic Types of Thyroid Cancers and Their Respective Abilities to Store Radioactive Iodine as Demonstrated by Radioautograms, Brookhaven Conf. Report on Radioactive Iodine, July 28-30, 1948. (*h*) Dobyns, B. M.: Thyroid Nodules Benign and Malignant: Observations on Their Functions, M. Clin. North America **33**: 1225, 1949. (*i*) Fitzgerald, P. J., and Foote, F. W.: The Function of Various Types of Thyroid Carcinoma as Revealed by the Radioautographic Demonstration of Radioactive Iodine (I^{131}), J. Endocrinol. **9**: 1153, 1949.

12. (*a*) Seidlin, Rossman, Oshry, and Siegel.[5b] (*b*) Leiter, Seidlin, Marinelli, and Bauman.[13c] (*c*) Seidlin, S. M.; Oshry, E.; Yalow, B. S., and Yalow, A. H.: Spontaneous and Experimentally Induced Uptake of Radioactive Iodine in Metastases from Thyroid Carcinoma: A Preliminary Report, J. Clin. Endocrinol. **8**: 423, 1948.

13. Unpublished data. Rall, J. E.; Keating, F. R.; Marschelle, H. P., and Bennett, W. A.: Distribution of Radioiodine in Patient with Thyroid Cancer, J. Clin. Endocrinol. **9**: 1379, 1949.

Clinical Notes, Suggestions and New Instruments

PRIMARY CARCINOMA OF THE NAIL

LYLE W. RUSSELL, M.D.
Peoria, Ill.

In 1939 Levine and Lisa[1] stated that primary carcinoma of the nail is one of the rarest manifestations of malignant disease. They reviewed the literature and found only 17 proved and 2 probable cases reported, nearly all of which were in foreign literature. Of the 19 patients 11 were men, 7 women and 1 unknown. Ten had a history of injury followed by a period of six months to eighteen years before diagnosis of cancer. The type of trauma was described as a deep puncture wound between the nail and the nail bed. In 13 of the 19 cases the lesions were in the hand, and, of these, nine were in the right thumb or index finger. Pain was prominent in only 7 cases. The diagnosis in 16 cases was squamous cell carcinoma, in 2 cases basal cell carcinoma and in 1 case papilloma. In only 4 cases was mention made of the presence or absence of bone involvement: in 1 it was absent; in 2 there was pressure erosion, and in 1 there was invasion. Metastasis was seldom mentioned.

Fig. 1.—Roentgenograms of the index finger, showing swelling of the soft tissue and destruction of the bone of the terminal phalanx.

A review of the literature since 1939 reveals no additional reports on cases of primary carcinoma of the nail. The apparent rarity of this lesion, particularly when it is associated with erosion of bone, prompts the report of this recent case.

REPORT OF CASE

C. S., a 37 year old white laborer, noticed the gradual development of a "sore" on the lateral edge of the nail of his right index finger in May 1949. Two months later the end of the finger gradually became swollen but not painful. About two weeks after the onset of swelling he consulted his family physician, who made a presumptive diagnosis of paronychia. He therefore made an incision along the lateral border of the finger, but, instead of obtaining purulent material, he encountered only a white cheesy substance. None of this material was

1. Levine, J., and Lisa, J.: Primary Carcinoma of the Nail, Arch. Surg. **38**: 107 (Jan.) 1939.

saved for microscopic study. The incision wound healed promptly, and four days later the patient was referred to me for consultation.

Examination revealed a large bulbous swelling of the distal end of the right index finger, which was only moderately tender to pressure. The skin was pink and shiny. In the sulcus of the nail, on the radial side of the finger, there was a small crater, about 5 mm. in diameter, filled with a yellowish crust. No fluctuation could be felt, and there was no increased warmth as compared to the contiguous skin. There were no palpable axillary or antecubital lymph glands.

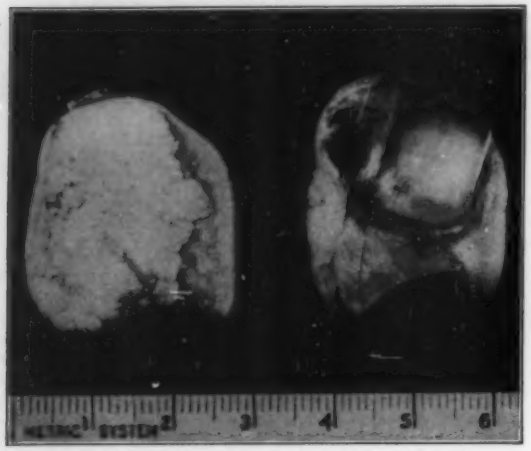

Fig. 2.—The distal portion of the amputated finger. At the left is a longitudinal section showing the tumor mass, which has eroded the bone. On the right an incision has been made along the edge of the nail to show the crater-like lesion in the sulcus.

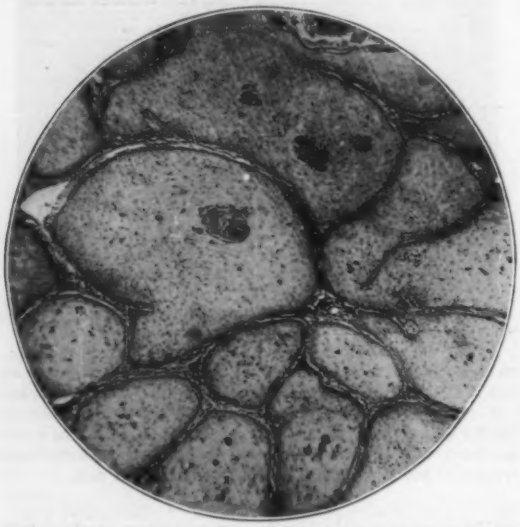

Fig. 3.—High power photomicrograph which shows the typical picture of a squamous cell carcinoma with cornification.

Further questioning of the patient brought out the fact that in August 1948 (nine months prior to the appearance of the "sore") the right index finger had been pinched by an air hammer. This, however, seemed only a minor incident to him at the time. There had been no history of any trauma since that time.

Roentgenograms (fig. 1) revealed swelling of the soft tissue involving the terminal end of the right index finger and considerable bone loss along the lateral surface of the terminal phalanx involving all except the extreme tuft and the articular margin. A roentgenogram of the chest showed only calcification in the left hilum and fibrous scarring above this level. Routine blood and urine examinations showed normal conditions.

The patient was hospitalized, and, with the patient under procaine hydrochloride block anesthesia, an amputation was performed through the distal interphalangeal joint. On the radial side of the finger there was a large, well defined mass of white caseous material extending from the ulcerated area on the skin down to and eroding about one half of the bone of the terminal phalanx (fig. 2). There was no pus. This mass had the gross appearance of a carcinoma, and, since the line of amputation was just proximad to the margin of it, additional soft tissue and the distal one half of the second phalanx were excised. The wound was closed with two short skin flaps. Microscopic examination of sections through the center of the tumor mass showed the typical picture of squamous cell carcinoma with pronounced cornification (fig. 3).

The wound healed by first intention, and, at the time of this writing, eight and one-half months after amputation, there has been no evidence of local recurrence in the stump or metastasis to the regional lymph nodes. The patient now has a useful stump of the index finger.

COMMENT

Diagnosis.—The appearance of the lesion in the sulcus of the nail is the most distinguishing characteristic of carcinoma of the nail. However, its significance may be minimized when decided swelling of the finger and erosion of the bone are present. Hence, it may become confused with the following conditions:

1. Chronic Paronychia: In chronic paronychia the pain is usually more intense than it is in carcinoma and there is an increased warmth and redness of the skin. Fluctuation can be felt in the finger, and incision yields a purulent drainage.

2. Tuberculous Dactylitis: Tuberculous dactylitis is characterized by the gradual onset of a fusiform swelling of the finger which is only occasionally painful. Roentgenograms show an expansion of the bone, with a cyst-like cavity in the center. A strongly positive reaction to the tuberculin skin test is suggestive but not diagnostic. As the disease progresses, a cold abscess may form and then erupt on the surface. However, in the earlier stages a diagnosis may have to be made on smear, culture and, possibly, inoculation of guinea pigs with the purulent, caseous material obtained by incision and drainage.

3. Syphilitic Dactylitis: Syphilitic dactylitis occurs chiefly in children and is more common in the proximal phalanges. Roentgenograms may show expansion and absorption of bone, but the new bone formation is a distinguishing characteristic. The finger is swollen but not painful. The reaction to the Wassermann test is positive. Usually there are other evidences of syphilitic infection.

4. Glomus Tumor: In cases of glomus tumor the roentgenograms may show a cystic appearance of the bone, but the clinical features are severe pain, red discoloration and, sometimes, recurrent vesicles of the skin and a slight swelling of the finger.[2]

5. Enchondroma: Enchondroma is characterized by a uniform expansion of the phalanx. The roentgenogram shows rarefaction which is centrally located, but a thin cortex is usually preserved.

Pathogenesis.—The possible relationship of trauma as an inciting cause in the formation of carcinoma of the nail may be a subject of much debate—especially in settlement of industrial compensation cases. Although no one can definitely prove that trauma has been the sole cause, certainly the evidence which has been obtained in the cases reported in the literature would tend to give the employee the benefit of the doubt. In 10 of the 19 cases reported by Levine and Lisa[1] there had been a history of injury. Bick,[3] in 1936, stated that trauma plays a large part in producing primary carcinoma of the extremities.

2. Lattes, R., and Bull, D.: A Case of Glomus Tumor with Primary Involvement of Bone, Ann. Surg. **127:** 187 (Jan.) 1948.

3. Bick, E.: Primary Carcinoma of the Extremities, Ann. Surg. **103:** 410 (March) 1936.

The question of infection as a possible inciting factor has been raised by Silverman,[4] who, in 1935, reported an epithelioma resulting from a chronic paronychia in which the nail had been removed twice. According to most observers,[5] all primary carcinomas of the extremities are of low grade malignancy and metastasize slowly only by way of regional lymph nodes.

Treatment.—Amputation is generally conceded to be the treatment of choice, but the site of amputation and the necessity of supplementing it with roentgen therapy are debatable points. I will probably be subject to criticism by some for not amputating the entire finger, or at least through the midjoint, in this case. However, the loss of an entire index finger is a serious disability to a workman; even the presence of a midjoint aids in the gripping power. Since the amputation line appeared to be well proximad to the tumor and since the tumor is locally invasive and metastasizes slowly to the regional lymph nodes, it was felt that it was safe to preserve as much of the finger as possible. If, at any of the frequent examinations during the ensuing months, there is evidence of local tumor growth in the stump, then the remainder of the finger will be amputated. If any enlargement of the regional lymph nodes is noted, they will be dissected. A roentgenologist was consulted on this case, and he was of the opinion that roentgen therapy should await some indication of incomplete cure by amputation. Fortunately the prognosis for cure after amputation is good, and seldom has a recurrence been noted, unless metastasis has already occurred prior to amputation.

AUREOMYCIN HYDROCHLORIDE IN ACTINOMYCOSIS

LOUIS T. WRIGHT, M.D.
and
HARRY J. LOWEN, M.D.
New York

With the advent of the sulfonamide drugs and, later, penicillin the prognosis in actinomycosis took a brighter turn. Several reports appeared in various journals on the success of treatment

Fig. 1.—Appearance of lesions before treatment.

with the aforementioned agents. Dobson and Cutting [1] reported their results in 12 cases, and they concluded that both penicillin and the sulfonamide compounds are highly effective in the treatment of actinomycosis. Hendrickson and Lehman [2] in 1945 reported on the successful treatment by penicillin of cervicofacial actinomycosis without surgical drainage. In 1948, Nichols and Herrell [3] gave their results in the treatment of this disease. Glover, Herrell, Hillman and Pfuetze [4] gave a good

Fig. 2.—Appearance of lesions before treatment.

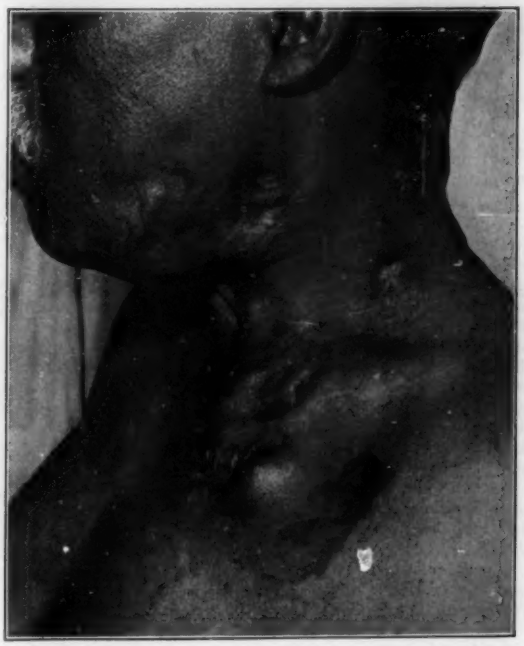

Fig. 3.—Appearance of lesions seven days after the start of treatment.

4. Silverman, I.: Epithelioma Following Chronic Paronychia, Am. J. Surg. **29**: 141 (July) 1935.
5. De Bell, P. J., and Stevenson, T. D.: Squamous Cell Epithelioma of the Extremities, Surg., Gynec. & Obst. **63**: 222 (Aug.) 1936. Levine and Lisa.[1] Bick.[2]

From the Surgical and Medical Services of Harlem Hospital.
Dr. William H. Hayling and Mr. Philip Steinberg assisted in this case.
The aureomycin hydrochloride was supplied by the Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

1. Dobson, L., and Cutting, W.: Penicillin and Sulfonamides in Actinomycosis, J. A. M. A. **128**: 856 (Nov. 24) 1945.
2. Hendrickson, G. G., and Lehman, E. P.: Cervicofacial Actinomycosis Successfully Treated by Penicillin Without Surgical Drainage, J. A. M. A. **128**: 438 (June 9) 1945.
3. Nichols, D. R., and Herrell, W. E.: Penicillin in the Treatment of Actinomycosis, J. Lab. & Clin. Med. **33**: 521 (May) 1948.
4. Glover, R. P.; Herrell, W. E.; Hillman, F. R., and Pfuetze, K. H.: Nocardiosis, J. A. M. A. **136**: 174 (Jan. 17) 1948.

review of the literature in addition to their results, and Campbell and Bradford [5] noted the excellent prognosis in their cases by treatment with sulfonamide drugs and penicillin. More recently, Weed and Baggenstoss [6] reported on the pathologic and bacterial studies of 21 fatal cases and the history of the disease and difficulty in diagnosis. We have not been able to find, after a careful search of the literature to date, any report on the use of aureomycin in the treatment of actinomycosis.

Fig. 4.—Condition at the end of three weeks: all swelling of the face and neck had disappeared.

REPORT OF CASE

A Negro aged 72 was admitted to Harlem Hospital with weakness of his left arm and leg on September 13, 1949. In 1927 the patient had noticed a swelling on the left side of his jaw and neck with draining sinuses, which had persisted to the present. His past history was otherwise noncontributory. Essential physical observations were hemiparesis of his left arm and leg. His blood pressure was 194 systolic and 96 diastolic, and reaction of the blood to the Wassermann test was strongly positive. Cataracts and primary optic atrophy were present in both eyes. On local examination there was a nodular swelling in the left mandibular and supraclavicular areas, and in the same region there were multiple draining sinuses. The tumefaction was nontender but hard and lumpy.

Smears from the draining sinuses on Sept. 14, 1949 revealed sulfur granules with (when crushed and stained) the typical structure of the ray fungus Actinomyces bovis. Culture revealed Actinomyces israeli.

Biopsy on skin and underlying subcutaneous tissue obtained with the patient under local anesthesia on Sept. 19, 1949 revealed granuloma with suppuration.

On September 22 the patient was given aureomycin hydrochloride, 0.5 Gm. every six hours by mouth. Within six days the draining sinuses had healed and the masses were much smaller. At the end of two weeks all cervical nodes were no longer palpable; at the end of twenty days the mass under the left side of the jaw and on the left side of the neck had entirely disappeared.

5. Campbell, D. A., and Bradford, B., Jr.: Actinomycosis of Thoracic Abdomen, Arch. Surg. **57**: 185 (Aug.) 1948.

6. Weed, L. A., and Baggenstoss, A. H.: A Pathologic Study of Twenty-One Fatal Cases, Am. J. Clin. Path. **19**: 201 (March) 1949; Some Problems in the Diagnosis of Actinomycosis, Proc. Staff Meet., Mayo Clin. **24**: 463 (Aug. 31) 1949.

SUMMARY

1. A case of actinomycosis is reported in which aureomycin hydrochloride was used with dramatic results. Six weeks after cessation of therapy there had been no recurrence.

2. Aureomycin is an additional drug that apparently has value in the treatment of actinomycosis.

3. No case of actinomycosis treated with aureomycin was found in the literature.

STRANGULATED DIAPHRAGMATIC HERNIA COMPLICATING DELIVERY

SEIBERT C. PEARSON, M.D.
STIRLING G. PILLSBURY, M.D.
and
MacWINSTON McCALLUM, M.D.
Long Beach, Calif.

Thompson and LeBlanc [1] in 1945 reported the first case of successful repair of a strangulated diaphragmatic hernia occurring immediately after delivery. We wish to report a second similar case.

REPORT OF CASE

Mrs. L. B., a 31 year old white woman, gravida 1, entered the Seaside Memorial Hospital at 6 a. m. on Feb. 25, 1949. Her past history was without significance. She had always

Fig. 1.—Upright bedside roentgenogram showing depression of the right side of the diaphragm; the left side is not identified. There is homogenous increased density in the lower left side of the chest. Air-containing intestinal loops are present in upper left side of the chest. The mediastinum is shifted to the right.

Drs. Pearson and Pillsbury are Fellows of the American College of Surgeons.

Drs. A. H. Buell and H. J. Prichard of the Medical and X-Ray Departments aided in this study.

From the Surgical Department (Dr. Pearson) and the Obstetrical Department (Drs. Pillsbury and McCallum) of Seaside Memorial Hospital, Long Beach.

1. Thompson, J. W., and LeBlanc, L. J.: Congenital Diaphragmatic Hernia, Visceral Strangulation Complicating Delivery, Am. J. Surg. **67**: 123, 1945.

been active and had participated in athletics. She gave birth to a viable female child at 1:40 p. m., after a seven hour labor. A low spinal anesthetic was given when the head crowned.

After returning to her room, the patient was comfortable and her condition was excellent. About seven hours after delivery she began complaining of a cramp-like intermittent pain in the

Fig. 2.—Upright lateral roentgenogram showing dilatated stomach with air-fluid level in anterior part of the chest. There are multiple air-filled loops of intestine throughout. The thick gastric wall suggests edema.

left upper part of the abdomen and the left posterior part of the chest. There was some nausea. About four hours later the pain increased in severity and the patient vomited twice. Physical examination at this time revealed dulness over the left posterior part of the chest and diminished breath sounds. Active peristalsis was heard in the lower two thirds of the left side of the chest. Blood pressure was 110 systolic and 70 diastolic. The pulse rate was 76, respiratory rate 18 and temperature 98.6 F. Morphine sulfate ¼ grain (15 mg.) was given, and a roentgenogram of the chest was made with a portable unit (fig. 1). The patient was then taken to the roentgenography department and supplemental films were made (figs. 2 and 3). The patient was seen by one of us at 4 a. m., and, after a review of the history and roentgenograms and with the report of Thompson and LeBlanc in mind, immediate surgical intervention was advised.

While preparations for surgical intervention were being made, the patient's blood was typed and cross-matched. A Levin tube was passed into the stomach, and a moderate amount of clear, colorless fluid was aspirated. At 5 a. m., with the patient under spinal anesthesia supplemented with nitrous oxide and oxygen, the abdomen was entered through an upper left rectus incision (the patient was prepared and draped for a thoracic extension of the incision if necessary). Only the descending colon and spleen were found in the peritoneal cavity, the remainder of the gastrointestinal tract being in the left pleural cavity. A defect in the posterolateral portion (pleuroperitoneal hiatus) of the diaphragm 7 cm. in diameter was found. It was necessary to enlarge the opening before the abdominal organs could be returned to the peritoneal cavity. The left lung was completely collapsed. The gastric wall was engorged, edematous and hemorrhagic, as was also the greater omentum. The stomach had rotated in such a manner that the pylorus and cardia were obstructed, as, immediately after reduction, the Levin tube drained a large quantity of serosanguineous fluid containing bile. The hernia was of the congenital type, no sac being present. Because of the recent pregnancy the peritoneal cavity easily accommodated the returned organs. The edges of the diaphragmatic defect were freshened, and the diaphragm was closed with interrupted sutures of number 20 cotton. Five hundred cubic centimeters of 5 per cent dextrose in water and 500 cc. of whole blood were given during the operation. The patient was in good condition after the operation.

A roentgenogram of the chest the day after operation showed the left lung almost completely collapsed. A roentgenogram on the fifth day after operation showed almost complete reexpansion of the left lung. The Levin tube was removed on the fourth day after operation. The patient had a satisfactory convalescence and was discharged on the tenth postpartum and the ninth postoperative day. Figure 4 is a roentgenogram of the patient's chest taken June 13.

Undoubtedly in this patient the hernia had been present from birth, and the left lung had functioned little if at all. We cannot imagine a sudden collapse of one lung occurring with so few respiratory symptoms. There was no evidence of any recent trauma to the left side of the diaphragm. It is probable that some or all of the abdominal organs migrated at times into the left pleural cavity and that during labor these organs were forced more violently into the chest and retained there, allowing obstruction to develop.

COMMENT

Several fatalities due to strangulated diaphragmatic hernia complicating delivery have been recorded, and there are doubtless many more which have not been reported. Diddle and Tidrick[2] in 1941 reported a fatality in a 23 year old woman during her fourth labor. The patient had had two normal deliveries subsequent to the discovery of a diaphragmatic hernia. These authors were able to find 4 fatal cases recorded in the

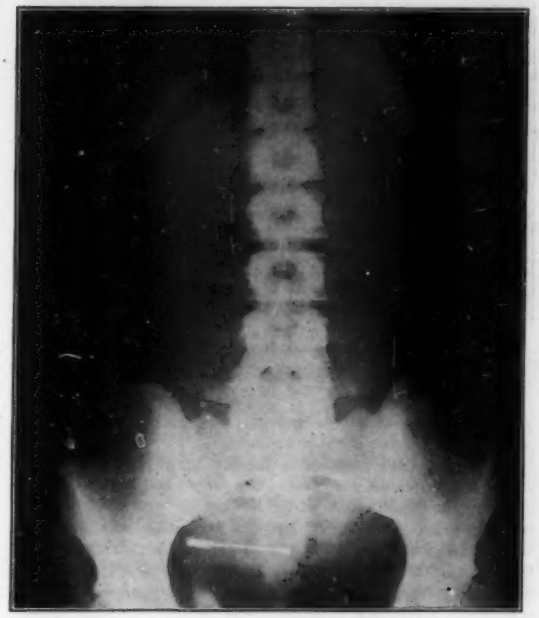

Fig. 3.—Flat of abdomen. The left side of the diaphragm is elevated. There is no intestinal gas except in the descending colon.

literature. We have been able to find 2 other fatal cases of strangulated diaphragmatic hernia associated with pregnancy and consider them pertinent to the subject.

Fishbach[3] in 1928 reported a fatality occurring a few days post partum. The patient was a 26 year old married woman.

2. Diddle, A. W., and Tidrick, R. T.: Diaphragmatic Hernia Associated with Pregnancy, Am. J. Obst. & Gynec. **41**: 317, 1941.
3. Fishbach, H. R.: A Fenestra of the Diaphragm, Arch. Path. **6**: 867 (Nov.) 1928.

The past history was noncontributory. She had given birth to her first child without complication eighteen days before the onset of her fatal illness. Four days after returning home severe knifelike pains began suddenly in the lower lumbar region on both sides, radiating upward between the shoulder blades. Accompanying these were intermittent cramping pains in the lower part of the abdomen, like uterine contractions. The pains continued until relieved by morphine, but they never disappeared entirely. Nausea was more or less constant, with occasional vomiting. The patient was admitted to a hospital three days after onset.

Physical examination was recorded as normal. The pain in the lumbar region was diffuse and continued to be severe. The patient vomited once. At midnight she was seen by a nurse and was apparently all right. Fifteen minutes later she was found dead on the floor.

At autopsy an opening 11 cm. in diameter was found in the left dome of the diaphragm. The edges were smooth, rounded and fibrous, without evidence of any fresh tear. All the gastrointestinal tract except the sigmoid colon was in the pleural cavity, as were the spleen and pancreas. The stomach was greatly dilatated with fluid and gas, and the abdominal viscera were decidedly congested with blood.

Fig. 4.—Anterior upright roentgenogram showing slight depression of the right side of the diaphragm and slight elevation of the left. The heart is shifted to the left. There is no collapse or fluid and no hernia.

Yenen [4] in 1946 reported a fatality in a 17 year old girl who was six months pregnant. The illness had begun ten days previously with acute pain in the left side of the chest and dyspnea. She had been under hospital treatment for "pleurisy." Nausea and vomiting had been present for three days when she was transferred with a diagnosis of vomiting of pregnancy. The left side of the chest was splinted, and breath sounds were not heard. The heart impulse was under the right breast. Dehydration and acidosis were present. The dyspnea was ascribed to pleural effusion, but three attempts at thoracentesis were unsuccessful. An 880 Gm. fetus was aborted by the patient on the night of her admission to the second hospital. The pulse then became weak and fast; dyspnea was more apparent, and cyanosis increased. The patient died in the early hours of the morning.

At autopsy a hernia of the left side of the diaphragm 5 cm. in diameter was found. The stomach and all the intestines except the colon were in the chest. Fat necrosis was present. The small intestines showed areas of infarction.

Strangulated diaphragmatic hernia has a high mortality. Carter,[5] in a collected series of cases from 1798 to 1945, found a general mortality of 72.9 per cent and an operative mortality of 54.8 per cent. Early diagnosis and definitive surgical intervention is imperative, as resection of gangrenous or nonviable bowel greatly increases the mortality. To suspect the condition in cases of pain in the upper part of the abdomen and nausea and vomiting will lead to early diagnosis. Roentgen examination of the chest is the one most important diagnostic aid, but Gibson [6] has stressed the following diagnostic points: (1) diminished expansion of the chest; (2) impairment of resonance; (3) adventitious sounds; (4) cardiac displacement; (5) circulatory collapse; (6) cyanosis, and (7) asymmetry of the hypochondria.

Carter and Giuseffi [5] stress the following observations on roentgen examination: (1) simulation by the herniated viscus of "high diaphragm"; (2) cardiac shift to the right (does not accompany high diaphragm normally and is not apt to be present unless there are considerable amounts of fluid or viscera in the thorax); (3) the presence of an air bubble above the normally anticipated level of the diaphragm, and (4) evidence of fluid in the chest.

In general we believe that the combined abdominal and thoracic approach should be employed in the treatment of strangulated diaphragmatic hernia; however, in the case reported here the recent delivery made the exposure and repair through the abdomen an easy procedure.

There is an increasing use of the miniature roentgenogram of the chest on all hospital admissions. However in the obstetric department the making of this film is usually deferred until after delivery. In view of our experience and that of others it would seem desirable to arrange for the pregnant patient to have roentgenograms made of her chest some time prior to the expected date of delivery. It is doubtful that surgical intervention would be recommended for the occasional patient with diaphragmatic hernia so discovered, yet one would be cognizant of the condition and an early diagnosis would have been made should symptoms of strangulation develop.

SUMMARY

A case of strangulated diaphragmatic hernia complicating delivery is reported. This is believed to be the second patient with this condition operated on successfully. Some of the important diagnostic points are mentioned. It is suggested that, where miniature roentgenograms of the chest are taken routinely, pregnant women have roentgenograms made of their chests as soon as possible after entering the hospital.

4. Yenen, E.: Diaphragmatic Hernia Complicating Pregnancy, Türk tib. cem. mec. **12**: 236, 1946.

5. Carter, B. N., and Giuseffi, J.: Strangulated Diaphragmatic Hernia, Ann. Surg. **128**: 210, 1948.

6. Gibson, F. S.: Diagnosis of Diaphragmatic Hernia with Acute Obstruction, J. A. M. A. **93**: 1719 (Nov. 30) 1929.

Patents, Commissions, Rebates and Secret Remedies.—An ethical physician will not receive remuneration from patients on or the sale of surgical instruments, appliances and medicines, nor profit from a copyright on methods or procedures. The receipt of remuneration from patents or copyrights tempts the owners thereof to retard or inhibit research or to restrict the benefits derivable therefrom to patients, the public or the medical profession. The acceptance of rebates on prescriptions or appliances, or of commissions from attendants who aid in the care of patients, is unethical. An ethical physician does not engage in barter or trade in the appliances, devices or remedies prescribed for patients, but limits the sources of his professional income to professional services rendered the patient. He should receive his remuneration for professional services rendered only in the amount of his fee specifically announced to his patient at the time the service is rendered or in the form of a subsequent statement, and he should not accept additional compensation secretly or openly, directly or indirectly, from any other source.

The prescription or dispensing by a physician of secret medicines or other secret remedial agents, of which he does not know the composition, or the manufacture or promotion of their use is unethical.

From the PRINCIPLES OF MEDICAL ETHICS of the American Medical Association.

Special Article

STANDARDS OF EFFECTIVE ADMINISTRATION OF INHALATIONAL THERAPY

Second Report by the Committee on Public Health Relations of the New York Academy of Medicine

Recent extension of knowledge concerning the physiology of respiration and the development of improved methods of administering inhalational therapy have made it advisable to review the "Standards of Effective Administration of Inhalational Therapy" formulated by the Committee on Public Health Relations of the New York Academy of Medicine in 1943.[1] It has also seemed appropriate to emphasize again the importance of observing these standards in the everyday practice of inhalational therapy.[2]

INHALATIONAL AND PHYSIOLOGICALLY DIRECTED THERAPY

The importance of inhalational therapy in modern medical practice has been shown by its effective use in cardiac failure, coronary artery disease, asthma, atelectasis of the lungs in the newborn, postoperative atelectasis, pneumonia, pulmonary edema, emphysema and cerebral thrombosis, as well as by its value in the treatment of war gas poisoning, respiratory failure due to poisons and other causes, drowning, severe hemorrhage, acute altitude sickness and shock.

The therapeutic use of oxygen is based on the existence of a state of anoxia, that is, lack of oxygen in the tissues. This may be produced by failure of an adequate pressure of oxygen to reach the pulmonary capillaries or by a lowered blood flow which causes a disproportionately large amount of oxygen to be taken out of the capillaries and which results in a diminished oxygen pressure insufficient for normal functioning of the tissues. Oxygen want may develop even with a normal arterial saturation, as in a thrombosis of the coronary, popliteal or cerebral arteries. Treatment in these circumstances makes use of the increased pressure of oxygen physically dissolved in the blood, an accomplishment which not only increases the tension of oxygen through an artery that still may be partly patent but, more significantly, raises the tension in the collateral circulation which feeds the area of the obstructed artery. The most pronounced signs of the physiologic advantages of inhalation of oxygen are a diminution in cyanosis, dyspnea, the pulse rate, restlessness and delirium and a decrease in the volume of pulmonary ventilation.

Although the administration of oxygen is the mainstay of inhalational therapy, other procedures have been developed to improve respiratory function. These include the employment of helium with oxygen, and of oxygen or helium-oxygen mixtures under positive pressure. The usefulness of substituting helium for nitrogen in a respirable gas mixture is due to the lower specific gravity of helium; this property makes it possible to breathe through constricted pulmonary passageways at almost one half the effort required for respiration of air or of pure oxygen. The decreased physical pressure necessary for the inhalation of a helium-oxygen mixture results in a lowering of the elevated negative pressure that occurs within the chest in obstructive dyspnea except in the presence of emphysema. Positive pressure provided during inspiration tends to prevent the excessive negative intrapulmonary pressure from exerting a suction action on the bronchial and pulmonary epithelium and thus is apt to inhibit the collection of excessive mucus within the bronchi and the development of pulmonary edema. Positive pressure within the lungs during expiration precludes severe bronchial constriction and may in some cases retard the flow of blood into the right auricle, allowing the heart to deal temporarily with a smaller volume of blood. In addition, positive pressure breathing exerts an opposing pressure on the external capillary wall, tends to prevent edema and counteracts the internal hydrostatic pressure within the capillary.

The local application of epinephrine and phenylephrine hydrochloride by inhalation of nebulized mists brings these agents in contact with the smaller bronchi locally and frequently brings about cessation of bronchial spasm and a decreased swelling of the mucous membrane at a relatively low concentration of the drug in the body. In recent years antibiotic aerosols have been used to combat infections in the respiratory tract; this phase of inhalational therapy is considered at length at the end of this presentation.

In order to regulate inhalational therapy properly, the physician should prescribe the concentration of oxygen and the volume flow per minute, as well as the type of apparatus and, in the newer procedures, the amount and type of positive pressure and the proportion of helium in helium-oxygen mixtures.[2]

APPARATUS FOR THE ADMINISTRATION OF OXYGEN

Cylinders and Regulators.—High pressure cylinders with a capacity of at least 220 to 244 cubic feet (6.2 to 6.9 cubic meters) or in the case of half-size cylinders 110 to 122 cubic feet (3.1 to 3.45 cubic meters) should be employed for the administration of oxygen. There is no justification for the use of low pressure tanks, since there is no special "medical" oxygen and only small quantities of oxygen can be furnished in this expensive manner. The oxygen used in medical practice is the same as industrial oxygen.

The pressure-reducing regulator attached to an oxygen cylinder contains two gages; the one proximal to the oxygen tank indicates the amount of gas in the tank and the distal one the rate of flow in liters per minute. Either a variable orifice float gage or a Bourdon tube spring type regulator gage may be employed, provided the gage chosen is made by a reliable standard manufacturer. The gage should be tested from time to time by measuring the rate at which the spirometer bell of a metabolism apparatus is filled at standard pressure and temperature. Before the regulator is attached to an oxygen tank, the oxygen cylinder should first be "cracked," that is, it should be opened slightly until the hiss of escaping gas is heard and then quickly closed. This is done to prevent the initial oxygen stream from

---

This article has been abbreviated in THE JOURNAL by omission of some of the illustrations. The complete article will appear in the reprints.

Prepared by Drs. Alvan L. Barach, Chairman, Clarence E. de la Chapelle, Bettina Garthwaite, Irving M. Pallin, Dickinson W. Richards Jr., H. McLeod Riggins, and Paul M. Wood, members, and E. H. L. Corwin, Ph.D., secretary, Subcommittee on Inhalational Therapy of the Committee on Public Health Relations.

1. Standards of Effective Administration of Inhalational Therapy, Committee on Public Health Relations of the New York Academy of Medicine, J. A. M. A. **121**: 755 (March 6) 1943. Barach, A. L.: Physiologic Therapy in Respiratory Disease, Philadelphia, J. B. Lippincott Company, 1948.

2. The results of a survey of the practice of inhalational therapy in hospitals, recently undertaken by the Committee on Public Health Relations of the New York Academy of Medicine, indicated a wide discrepancy between information available concerning methods of administration and the actual conduct of this form of therapy. The final results of this survey will be presented elsewhere.

blowing dust into the regulator. Oil should not come in contact with the regulator or cylinder valve either from oiling or from the technician's hands.

Oxygen Tents.—The oxygen tent is a comfortable and effective means of administering 50 to 60 per cent oxygen, provided precautions are taken to prevent undue leakage. The most important error in its use, one which is frequently made, is to allow the motor-driven fan to operate while the tent is opened for the patient to eat or drink or for the physician to examine the patient. It is of considerable importance to turn the motor off before the tent is opened or in ice-cooled tents before ice is added. If this is done, the amount of oxygen lost by diffusion is small and the loss from the refrigerating chamber is eliminated. After the patient has received attention, the tent is closed and the motor turned on again. When this procedure is used, a flow of 15 liters of oxygen a minute for twenty minutes, with a maintenance flow of 10 liters, results in an oxygen concentration within the tent of 50 per cent or higher in the majority of instances.

A maintenance flow of 10 liters of oxygen per minute should be used not merely to keep the concentration at 50 per cent but to wash out the carbon dioxide which

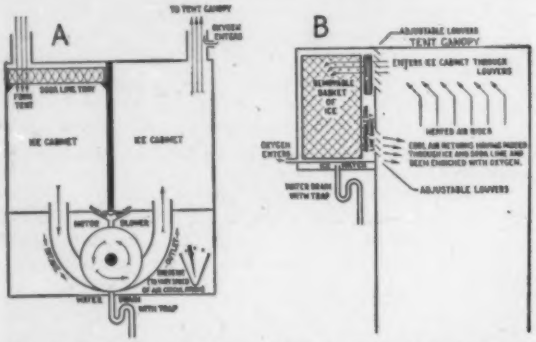

Fig. 2.—Circulation diagram of ice-cooled oxygen tents (*A*, motor blower tent; *B*, motorless tent). In the mechanically refrigerated tent a commercial refrigerant (freon®) is used with a compressor unit to accomplish air conditioning, with thermostatic regulation of temperature.

would otherwise accumulate in concentrations above 1 per cent, an undesirable amount. When a 60 per cent oxygen concentration is desired, the maintenance flow should be 12 to 14 liters per minute. In practice it is frequently advantageous to prescribe a flow of 12 liters per minute continuously, even for maintenance of an oxygen concentration of 50 per cent, since purging of the tent with 15 liters per minute is then usually not necessary. It is important, however, to test the concentration of a tent with an oxygen analyzer twice daily.

The technician should be equipped to test the carbon dioxide concentration in the tent. When it has been demonstrated that the percentage of carbon dioxide is not above 1 or at most 1.5 per cent under operating conditions, this test need not be performed routinely. The size of the tent does not mean that smaller flows of oxygen can be used. The patient who produces 200 cc. of carbon dioxide a minute must have this diluted with 20,000 cc. of air-oxygen mixture to keep the carbon dioxide concentration at 1 per cent. This is provided by leakage of air in and around the attachments to the bed of the transparent canopy as well as by an inflow of 10 or more liters of oxygen per minute. It is for this reason that soda lime is not needed in any properly constructed tent.

In the modern tent equipped with mechanical air-conditioning the temperature may be set at the desired level by employing the thermostat attached to the tent. It should be borne in mind that the tent does not have to be operated at low temperatures, but should be kept at that temperature which is comfortable to the patient and preferred by the physician.

For most patients with fever a temperature between 60 and 68 F. is preferred in winter and a slightly higher temperature in summer; for older patients and infants higher temperatures are often desirable. The relative humidity is generally maintained between 40 and 60 per cent. When tents are ventilated by motor blower circulation, which forces the oxygen-air atmosphere over ice or refrigerant (freon®)-filled coils, the humidity will usually be within this range. In certain conditions, such as tracheobronchitis, higher humidities and temperatures than are normally employed may be desirable. Nebulizers or vaporizers may be employed to add water to the atmosphere. The technicians should be instructed to observe and record the temperature in the tent at each visit. If the temperature rises above 70 F., the indication is that there is inadequate cooling and consequently inadequate removal of moisture.

Tents for Infants: The same general principles apply to tents for infants, except that higher temperatures and higher humidities should be prescribed for very young infants. Furthermore, smaller tents may be used. It should be recognized that infants deprived of heat by rapid circulation of cold atmosphere over them may have an abrupt fall in body temperature. A tent with an aperture at the top and with a means of admitting oxygen may be used, provided it is not placed near an open window or door where air currents may blow out the accumulated oxygen. It is desirable to test the oxygen concentration in these tents at the level of the infant's nose. Since infants produce little heat, water and carbon dioxide, an open-top tent without an air conditioner may be employed.

An injector meter may be employed for the administration of precise concentrations of oxygen of 40 to 90 per cent in both open box tents and closed head tents. The advantage of the injector is that it provides increased ventilation of the tent with adequate provision for washing out carbon dioxide; for example, a meter setting of 40 per cent oxygen results in an intake of 3 liters per minute of air for each liter per minute of oxygen. Charts are provided which indicate the proper rate of flow required to produce varying oxygen concentrations in both children and adults, as well as the flow required to wash out carbon dioxide in varying circumstances. These head tents may be used with or without ice by the provision of a rack at the back of the head.

Sterilization of the Tent: After the termination of use by each patient the tent should be washed with soap and water inside and outside. It should be finally rinsed with water or rubbed down with 70 per cent alcohol and thoroughly aired. In private practice the use of plastic canopies permits replacement. Ultraviolet lamps have been suggested as sterilizing agents.

Fire Hazards: All tents should be conspicuously labeled "Danger. No flames. No sparks." When a tent is used within a private room, it is desirable to place on the door a sign bearing a similar warning. Oxygen regulators should also be conspicuously stamped "Do not oil." It is suggested that noninflammable transparent material be used in the construction of tent canopies.

Smoking should not be permitted in a room in which an oxygen tent is being used. Electric heating pads or electric call bells should not be permitted within oxygen tents. Visitors should be warned by word of mouth to observe the regulations, as some do not know English or do not read the instructions.

Nasal Administration of Oxygen.—Nasal Catheters: There are several effective methods of administering oxygen through the nose: by means of a nasal catheter either in the nasopharynx or in the oropharynx, or by the use of double-bent nasal tubes which just enter the nostrils. The oxygen is first passed through approximately 3 inches (7.6 cm.) of water to prevent drying of the mucous membrane. A lubricated nasal catheter, no. 10 or 12 French, is inserted into the nostril for a distance of approximately 3 inches, that is, up to but not touching the posterior wall of the nasopharynx. Six liters of oxygen a minute generally provide 38 per cent oxygen in the inspired air. A single catheter may be used in one nostril at a time if irritation should occur. The terminal 1 inch (2.5 cm.) of the catheter should be perforated with four small holes in order to prevent a single stream of oxygen from impinging on one localized area of the mucous membrane.

If the catheter is passed down into the oropharynx opposite the glottis, a concentration of 42 per cent oxygen in the inspired air may be obtained at a flow of 6 liters per minute. When the catheter is used in the oropharynx, it is important to remember that oxygen may pass into the stomach and distend the abdomen if the catheter is placed lower than the uvula. With the catheter in the pharyngeal position, 7 liters of oxygen per minute may provide concentrations of 45 to 50 per cent oxygen if no sensation of discomfort is produced. When a patient, after insertion of the catheter in the oropharynx, swallows a bolus of air, the inference is that the catheter has been inserted too far; it should be withdrawn until the patient no longer swallows air.

In the use of the nasal catheter the instrument is generally placed in the nasopharynx, as this position is less complicated and safer than the oropharynx behind the uvula. Placement in the latter position admittedly results in a concentration of oxygen in the inspired air approximately 4 per cent higher than is the case with the nasal placement, but caution must be exercised constantly lest the catheter become lodged lower than the uvula; otherwise the stomach may become distended with gas. Furthermore, the administration of 6 to 7 liters per minute will maintain a concentration of at least 38 to 40 per cent oxygen in the average adult patient when the catheter is placed in the nasal pharynx. Mouth breathing lowers to some extent the oxygen percentage in the air inhaled, but this is not significant if breathing takes place through both nose and mouth.

The catheter should be lubricated with water soluble jelly and not with liquid petrolatum or petrolatum, since these are not absorbed by the lungs and may conceivably cause areas of lipoid pneumonitis if blown into the alveoli. It is probable that oil particles formed in this way are so large that they would not reach the alveoli, but this precaution is recommended. Furthermore, the catheter should be changed at six hour intervals to prevent the catheter from adhering to the side of the nasal passage after the lubrication is absorbed.

Double-Bent Nasal Tubes: The double-bent nasal tubes of rubber, more comfortable for most patients than the double metal nasal cannula, are serviceable in patients who do not tolerate the nasal catheter in the nasopharynx or the oropharynx. A flow of 7 liters per minute generally results in a concentration of 38 to 40 per cent oxygen.

Masks.—Oxygen masks are especially suitable for the intermittent administration of high concentrations of oxygen, from 50 to 100 per cent, and for helium-oxygen mixtures. The nasal catheter is generally more comfortable for long continued use and is just as effective as the oxygen mask when concentrations between 35 and 45 per cent are prescribed. Tents with transparent canopies and air-conditioning cabinets are generally more comfortable for the administration of concentrations between 50 and 60 per cent.

Within recent years it has become apparent that pure oxygen may be irritating to human pulmonary epithelium when administered by a mask continuously for an entire day and irritating to a slight extent in twelve hours. The fact that the mask is removed from time to time for various reasons may be responsible for the reported tolerance of 100 per cent oxygen. Warnings regarding the danger of pulmonary edema from inhalation of these high oxygen concentrations are also based on experiments on animals and human beings kept in airtight chambers continuously. Clinical and experimental evidence has recently indicated that concentrations of oxygen between 50 and 70 per cent have been used for long periods without damage to the lungs; on the basis of this evidence, a large increase in physically dissolved oxygen, provided by 70 per cent oxygen, may be used with great benefit in such conditions as shock, severe hemorrhage, widespread pneumonia and imminent cardiac failure.

There are two masks available, the B-L-B [3] and the Meter [4] mask. The B-L-B mask consists of a close-fitting rubber piece to cover the nose or the nose and mouth; from it is suspended a small bag in which a variable amount of rebreathing takes place. Two sponge rubber disks placed in the center of the mask serve as a combination inspiratory and expiratory valve. During inspiration the resistance in the sponge rubber prevents a free flow of air into the mask. When the rebreathing bag is emptied, air is drawn through the sponge disk. During expiration, the rebreathing bag is first filled with the exhaled air, and the remainder passes through the sponge rubber disk into the outer atmosphere.

During increased ventilation, as in severe dyspnea, the resistance imposed by breathing through the sponge rubber is materially enhanced. This is especially significant during the inspiratory cycle when flows of oxygen under 5 liters a minute are used; in some cases negative pressures within the mask have been recorded in excess of 2 cm. of water. It must also be pointed out that a rate of flow as low as 3 to 4 liters a minute will be accompanied with sufficient rebreathing to produce a carbon dioxide content of 2 per cent or higher in the inspired air; this high percentage of carbon dioxide aggravates the dyspnea of the patient by increasing the volume of breathing about 40 per cent. With the B-L-B mask it is therefore desirable to use a high flow of oxygen, from 7 to 10 liters per minute, in order to eliminate inspiratory resistance and the increased carbon dioxide concentration in the inspired air. For this reason it is impossible to give low oxygen concentrations with this mask without causing excessive rebreathing of

3. The B-L-B mask is named for its designers Boothby, Lovelace and Bulbulian.
4. Designed by A. L. Barach and M. Eckmann.

carbon dioxide and resistance due to the sucking of air through the sponge rubber disks.[5]

In the Meter mask a delicate inspiratory valve is placed between the mask and a large, light latex bag in which no rebreathing takes place; it simply serves as a collecting bag for oxygen. A light rubber flutter expiratory valve is placed in front of the mask for exit of the exhaled air. This mask operates with minimal resistance whether oxygen flow is high or low, provided the reservoir bag is not allowed to collapse completely. An injector is attached to the regulator, which makes possible the administration of oxygen concentrations of 40 to 100 per cent. By the use of apertures of different sizes in the injector, varying amounts of atmospheric air are sucked into the meter because of the negative pressure created by the stream of oxygen passing through it. Calibration of these orifices makes it possible to provide the desired oxygen concentration immediately with an error of not more than ± 3 per cent. If low rates of flow of oxygen and the exclusion of carbon dioxide from the inspired air are desired, the meter mask is the most suitable. Its use is also indicated in patients with obstructive dyspnea, because in these patients minimal inspiratory resistance is desirable. The rate at which oxygen flows from the regulator may be varied from 4 to 15 liters per minute, depending on the concentration desired and the volume of flow required to prevent the collecting bag from collapsing. The employment of less than 4 liters a minute is seldom indicated except for young children, for whom lower rates of flow may be adequate.

Although the masks are comfortable for some patients, it must be recognized that their continuous use becomes objectionable to many others. When discomfort prevents the continuous administration of oxygen by mask, a shift should be made to the oxygen tent, when feasible, or to nasal catheters, a hood or a face tent.

After use, the mask should be scrubbed thoroughly with soap and water and should be immersed or washed in a 70 per cent solution of alcohol.

Pressure Breathing.—Pressure breathing apparatus is of three general types:

1. Expiratory positive pressure breathing devices. These are simple appliances in which the patient exhales against a resistance, increasing the intrapulmonary pressure during expiration.

2. Continuous positive pressure breathing equipment. These types of apparatus provide continuous positive pressure in both inspiration and expiration.

In both these types the flow of air is continuous, and the patient breathes spontaneously.

3. Apparatus for artificial respiration. The simplest and most useful of these devices are those designed for intermittent positive pressure breathing, in which air or oxygen enters the lungs under positive pressure in inspiration; pressure is then automatically released, and expiration occurs as a passive act. Such apparatus is used in patients with depressed or failing respiration, as in coma or poisoning. Other apparatus for artificial respiration, of the "suck and blow" type, is also available.

The Oxygen Mask Metered for Positive Pressure: The Meter mask may be equipped with a metal disk which surrounds the expiratory flutter valve and contains on its external surface five orifices of different diameters. When the largest orifice is employed, expiration proceeds naturally without pressure. When the disk is turned to the smaller orifices, the patient exhales under a positive pressure of 1, 2, 3 or 4 cm. of water, depending on the size of the orifice and the volume of breathing. More accurate control of pressure is obtained when expiration is conducted through a water bottle calibrated in centimeters of water.

The use of positive pressure during expiration is specifically indicated for the treatment of acute pulmonary edema occurring in various conditions, such as pneumonia, left ventricular failure, some cases of shock and irritant gas poisoning. In oxygen therapy for patients with pulmonary edema it is customary to begin with pressure of 5 cm. of water and gradually lower it to 2 and then 1 cm. From 40 to 60 per cent oxygen is employed. The injector attached to the regulator is turned to the oxygen percentage desired, and the flow from the regulator is adjusted at that rate; this arrangement prevents the collecting bag from collapsing at the end of inspiration. It is desirable to have the injector one third full of water so that the stream of oxygen may pick up moisture as it passes into the mask. Distensible rubber bags which will provide some positive pressure in inspiration also are now being developed.

The relative humidity of pure oxygen passing at a flow of 8 to 10 liters a minute through the injector partially filled with water is approximately 20 per cent at 70 F. The inspired oxygen is additionally moistened by the inner surfaces of the mask, which are wet with the saturated water vapor resulting from expiration, so that the ultimate relative humidity of the inspired oxygen is approximately 45 per cent. If a still higher relative humidity is desired during inhalation of 100 per cent oxygen, the injector is removed and a water bottle attached to the regulator, so that the stream of oxygen will pass upward through at least 3 inches of water before entering the mask. However, air is usually employed in concentrations of 30 to 40 per cent, which contributes the moisture prevailing in the atmosphere.

Positive pressure is employed also to prevent or control the oozing that takes place from the tracheobronchial tree following tracheotomy. When this is used, the tracheotomy tube is prolonged so that expiration proceeds through an expiratory valve into a water bottle at pressures which generally begin at 4 to 5 cm. of water and are gradually lowered during a period of twelve hours to 1 to 2 cm. of water.

Positive pressure respiration should be administered cautiously in shock, in which the venous return to the heart is retarded, but increased intrapulmonary pressure of 2 to 4 cm. of water may be considered safe if plasma or blood is given concomitantly. When peripheral circulatory failure is suspected, the blood pressure should be followed at fifteen minute intervals and the intrapulmonary pressure reduced or discontinued if a fall greater than 10 mm. of mercury takes place in the systolic pressure after the application of breathing under positive pressure.

Continuous Pressure Breathing: Pressure breathing in inspiration and expiration is used for the treatment of asthma, for obstructive lesions in the larynx and trachea and for pulmonary congestion and edema. An effective device for pressure breathing in inspiration and expiration makes use of weights on two rubber bags into which 40 to 50 per cent oxygen is admitted from an injector; or, if desired, helium-oxygen mixtures may be used. A mask is employed in this apparatus, which is simpler although less comfortable for prolonged use than the positive pressure hood formerly employed.

5. It is regrettable that the advertising literature on the B-L-B apparatus continues to list oxygen flows of 3 to 4 liters per minute.

Inspiratory pressure may be built up swiftly by setting a specially constructed injector meter at a concentration of 40 per cent oxygen. This injector actually delivers 38 per cent oxygen, at a flow of 15 liters per minute, with a total gas flow of 65 liters per minute of air plus oxygen. With lower rates of flow, the building up of inspiratory positive pressure is less rapid.

Although pressures of 4 to 6 cm. of water are generally used for the treatment of obstructive dyspnea and pulmonary edema, higher pressures have been employed for brief periods in severe obstructive dyspnea and for resuscitation. When higher pressures are used, the effect on the circulation is more pronounced and may lead to a decrease in cardiac output, especially in patients with impaired circulation. In shock, positive pressure, when employed, should be used with the precautions that have been mentioned.

In obstructive dyspnea the greatest degree of relief is secured if an 80 per cent helium-20 per cent oxygen mixture is employed with pressure breathing. The injector is then not used, but a continuous flow of 7 to 9 liters per minute of the helium-oxygen mixture is provided.

The pressure breathing device described herein is also equipped with an emergency inspiratory valve, placed on the inspiratory side of the rubber tubing. Air may be introduced at any time through this valve, if the inspiratory collecting bag should for any reason collapse through the development of a leak. The patient is thus protected against breathing under a negative pressure.

Artificial Respiration: In respiratory failure, with depressed or inadequate respiratory stimulus, artificial respiration may be required. Such conditions include: poisoning with barbiturates, morphine, carbon monoxide and some of the more toxic alcohols; drowning, certain types of coma, poliomyelitis with respiratory paralysis and electrocution.

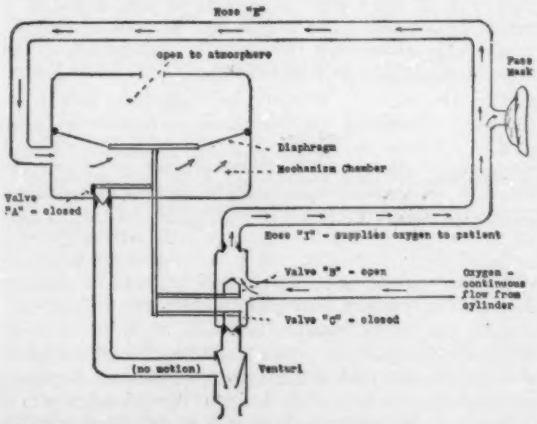

Fig. 13.—Emerson resuscitator, inhalation phase. Hose "I" carries only pure oxygen from the oxygen cylinder to the patient and never carries exhaled gases. This feature is covered by U. S. patent no. 2,268,172 and Canadian patent no. 405,705.

In any form of artificial respiration, with unconscious or stuporous subjects, special attention must always be given to clearing the airways. Mucus and foreign matter must be removed by suction or other means, the tongue kept well forward and the position of head and neck maintained in extension, with the chin somewhat elevated. In the presence of bronchospasm or respiratory tract edema, inhalation of bronchodilator drugs in the course of the artificial respiration may be useful. The even expansion of the chest during inspiration should be maintained at all times.

Manual methods of artificial respiration, such as the prone pressure (Schaefer) technic, do not provide adequate ventilation and are difficult or impossible to use

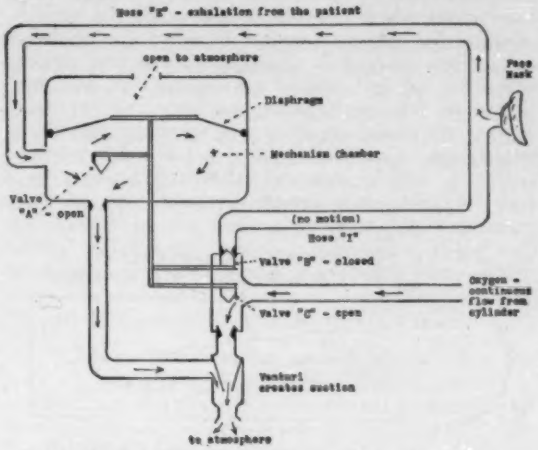

Fig. 14.—Emerson resuscitator, exhalation phase.

for prolonged periods.[6] The Eve rocking procedure is more effective but again difficult to apply in most clinical situations. An anesthesia bag and mask can be used for short periods, the operator compressing the oxygen-filled bag by hand to provide inspired air, and allowing expiration to occur passively. In this procedure there is usually enough leakage around the mask and enough flushing out of the bag with oxygen to prevent accumulation of carbon dioxide in the bag to any serious extent.

Special hand-operated intermittent positive pressure respirators are available. In these, air is forced into the chest by a hand bellows until a certain maximum pressure is reached (usually 10 to 15 mm. of mercury); then a valve is tripped, and the patient exhales passively into the outside air. The bellows is filled again from the air or from an oxygen tank, and the process is repeated. These forms of apparatus are useful for short periods.

For continued artificial respiration some type of automatic respirator is necessary. One of the practical difficulties with all such apparatus is to provide a tight-fitting mouthpiece or mask. Face masks with cushion rubber or inflatable rubber sides are the most widely used, but these must be strapped on tightly and constantly watched for displacement and leaks. In profound respiratory depression requiring hours or even days of continuous artificial respiration, intratracheal intubation by an anesthesiologist may be at times the best procedure.

The simplest artificial respirators are the intermittent positive pressure types. The essential features are an oxygen tank, a demand valve and a second, or cycling, valve. Air flows into the mask until a certain pressure is reached; then the inflow is shut off and expiration proceeds until the pressure in the mask is reduced to a certain low pressure (usually zero); then the

6. An effective method (J. H. Emerson) consists of raising and lowering the patient's hips while he is in the prone position.

cycling valve opens, oxygen flows from the demand valve and inspiration begins again. The pneumatic balance resuscitator is an effective form of this cycling apparatus, as are some of the other resuscitators. It should be emphasized that this apparatus will cycle also with the patient's own respiration, following recovery of his spontaneous inspiration and expiration; its operation thus differs from that of the Drinker type respirator, with which respiration is imposed.

Since intermittent positive pressure respiration provides a mean positive pressure over the respiratory cycle, it may be effective in reducing or preventing pulmonary edema in unconscious subjects. An intermittent positive pressure system has been used for as long as three days continuously, in a case of barbiturate poisoning, with maintenance of cardiopulmonary function. At the cycling pressures provided by this apparatus, there is in most cases no significant retarding effect on the venous return of blood to the heart.

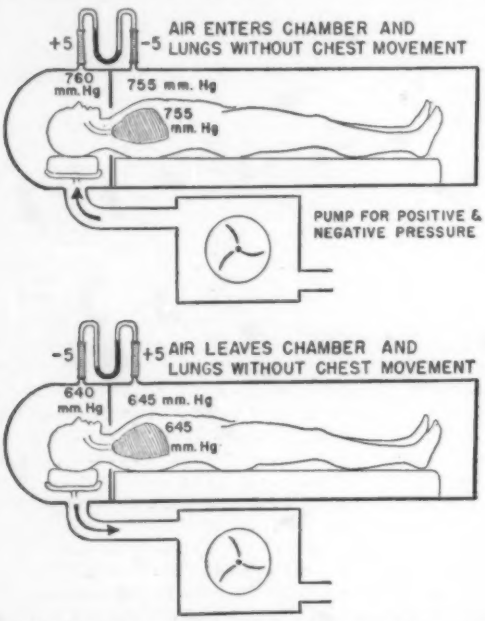

Fig. 15.—Pressure equalizing chamber provides lung ventilation without lung movement when pressures on outer and inner surfaces of chest wall are made equal by counterbalancing the resistance in the respiratory passageway.

The positive and negative pressure (suck and blow) respirators are also effective and safe to use with unconscious subjects. There is no convincing evidence that these forms of apparatus have deleterious effects either on the lungs or on the circulation. In fact, the mean average pressure, which is near zero, actually produces less impairment of venous return in patients with circulatory insufficiency. It should be noted that a rapid tripping indicates that oxygen is not reaching the alveoli because of some obstruction and that a slow tripping with coincident chest expansion indicates a good gaseous exchange. Slow tripping without adequate chest expansion may be due to a slow leak, usually at the point of application.

Some use has been made of respirators, especially the intermittent positive pressure types, on conscious subjects. In some instances, as when respiratory muscular exhaustion is severe or when pulmonary edema is present with relatively little dyspnea, the intermittent positive pressure respirator has been helpful in relieving symptoms. Generally, however, conscious subjects in need of respiratory aid are also dyspneic, requiring quick inhalation of air during the early phase of inspiration. Since most respirators cannot provide a rapid immediate volume of inflow, the patient inhales against a resistance in early inspiration, with a sensation of increased dyspnea or suffocation. Intermittent positive pressure respirators have been devised with an inflow capacity of extremely large volume (100 liters per minute) during early inspiration, but these are not commercially available at present.

The Pressure Equalizing Chamber: The pressure equalizing chamber provides an adequate exchange of gases within the lung by a swift variation in air density, accomplished by a change in pressure within the chamber of 120 mm. of mercury twenty-five times a minute. As air is first admitted into the head end of the chamber and then passes beneath a collar that surrounds the patient's neck, the pressure exerted on the outer surface of the wall of the chest is reduced to a degree that equals exactly the resistance in the respiratory passageway. Ventilation of the lung then proceeds without any change in lung volume.

This chamber has been used to immobilize the lungs in the treatment of chronic pulmonary tuberculosis; in recent studies it has been found that patients with obstructive dyspnea, such as those with intractable bronchial asthma and pulmonary emphysema, are promptly relieved of dyspnea during residence in the chamber. A varying higher pressure in the head end of the apparatus is required to overcome the increased resistance in the bronchial tubes. Additional pressure, greater than that required to overcome bronchial resistance, accomplishes pressure breathing at the start of inspiration. The patient may breathe without difficulty in a chamber of this type, since the differential pressure between the head and body ends of the chamber is generally not more than 3 or 4 mm. of mercury. Artificial respiration may therefore be conducted in an apparatus of this sort with or without positive pressure.

The Respirator: It should be recognized that maintenance of artificial respiration in a respirator is, in effect, achieved by positive pressure breathing. A negative pressure within the respirator of 12 mm. of mercury, which causes the lungs to expand, is equivalent to an increase in positive pressure on the face of 12 mm. of mercury. Since the pressure falls to that of the atmosphere in each instance, a mean average pressure, depending on the pressure curve, of 6 mm. of mercury is generally present. In other words, respiration conducted by the respirator, although it is induced by intermittent negative pressure within the chamber, is a form of intermittent pressure breathing in which inspiration is accomplished by a rise in pressure of 12 mm. of mercury and expiration by return of pressure to that of the atmosphere.

In most forms of intermittent pressure breathing hyperventilation is apt to take place. An increase in oxygen saturation resulting from loss of carbon dioxide does not contribute to the overcoming of anoxia, since a loss in the pressure of carbon dioxide in the tissues is in most instances approximately equivalent to a loss of oxygen pressure. With slight increases in pulmonary ventilation, the oxygen tension gained in this way may not be offset by the mild alkalosis engendered. In the

administration of intermittent positive pressure, therefore, precautions should be observed to prevent excessive loss of carbon dioxide by overbreathing. In contrast, the use of continuous pressure breathing is not accompanied with hyperventilation. The effect of the pressure used in continuous pressure breathing appears to be equivalent to the mean pressure of intermittent pressure breathings. For purposes of resuscitation, intermittent pressure breathing of some form is naturally indicated, and not continuous pressure respiration.

ADMINISTRATION OF HELIUM-OXYGEN MIXTURES

A mixture of 80 per cent helium with 20 per cent oxygen, which is employed in the treatment of asthma, obstructive lesions in the respiratory tract and pulmonary atelectasis in the newborn, may be administered in the positive pressure hood apparatus already described, but this requires skilled technical service and is generally too cumbersome for ordinary use. The usual

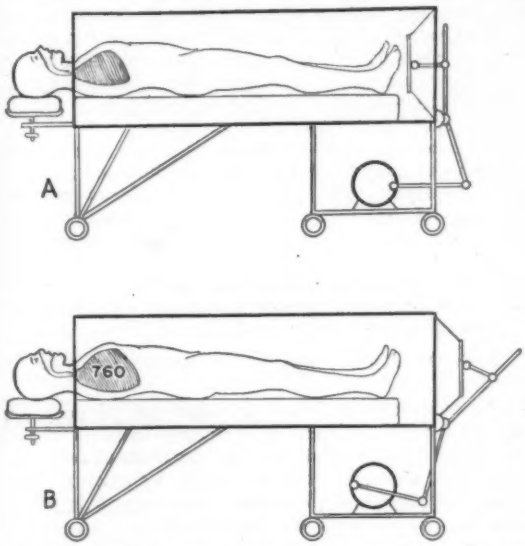

Fig. 16.—Artificial respirator. At the end of exhalation *(A)* the pressure both at the upper airway and surrounding the body is 760 mm. of mercury. Therefore no gradient exists between the pressure around the body and that at the nose and mouth. When a partial vacuum is created in the respirator (*B*) the pressure surrounding the body is 748 mm. of mercury and the pressure inside the patient's lungs is 760 mm. of mercury, greater than the pressure surrounding his thorax. The effect of this gradient is to cause inhalation as the thoracic cage is pushed out by pressure from within.

method of administering helium and oxygen is by the employment of a comfortable mask without rebreathing. Since inhalation of the helium-oxygen mixture is designed to relieve obstructive dyspnea, the slightest accumulation of carbon dioxide is a pronounced disadvantage, because an increase in the volume of breathing will correspondingly increase the effect of obstruction. Thus, if a patient is breathing at a pulmonary ventilation of 8 liters per minute, with a certain degree of respiratory obstruction, and the volume of breathing rises to 12 liters a minute as a result of the presence of 2.5 per cent carbon dioxide in the atmosphere, the pathologic effects of obstructive dyspnea are also increased 50 per cent. It is therefore desirable to use the meter mask, with the valve above the collecting bag, which prevents any rebreathing in the rubber bag. In most cases the mask may be used at atmospheric pressure with a flow of 7 to 8 liters as indicated on the ordinary oxygen regulator. It must be remembered that the flow indicated on the regulator should be multiplied by 1.7 in order to get the true flow of helium-oxygen mixture. In other words, the restricted orifice of the regulator is itself a demonstration of the higher rate of flow at a given pressure of a mixture of 80 per cent helium and 20 per cent oxygen.

More effective relief of obstructive dyspnea is provided by inhalation of helium-oxygen mixture under positive pressure during both inspiration and expiration; this relief may also be obtained by the device previously described that produces pressure as a result of a weight on both the inspiratory and expiratory collecting bags. The periodic inhalation of helium and oxygen under continuous pressure of 3 to 6 cm. of water is employed for the treatment of asthma, obstructive lesions in the respiratory tract and pulmonary edema. In the treatment of pulmonary edema it is desirable to reduce the pressure gradually, for example, about 1 cm. of water pressure at hourly intervals until the patient is breathing at atmospheric pressure.

ADMINISTRATION OF 5 TO 10 PER CENT CARBON DIOXIDE IN OXYGEN

The administration of 5 to 10 per cent carbon dioxide in oxygen is useful in carbon monoxide poisoning. Carbon dioxide-oxygen inhalation has also been employed in massive collapse of the lungs, in order to stretch the bronchi and perhaps loosen a tenacious plug of mucus, and for short periods after operations to expand the lungs and bronchi, but the evidence in favor of its value in the prevention and treatment of atelectasis has been questioned by many investigators. These carbon dioxide-oxygen mixtures should not, however, be left in a lung in or near the atelectatic state, since all these gases may be quickly absorbed and atelectasis thus rendered complete. In other words, atmospheric air (containing 79 per cent nitrogen) must be vigorously inhaled at the end of any treatment, in order to fill the alveoli with nonabsorbable nitrogen.

Carbon dioxide in oxygen is particularly useful in intractable hiccup. For this purpose a tank of 90 per cent oxygen and 10 per cent carbon dioxide may be employed with either a B-L-B or a meter mask for periods of two or three minutes or until the patient just loses consciousness. In some cases 15 per cent carbon dioxide for one and one-half to a maximum of two minutes produces better results. It must be borne in mind that prolonged administration of carbon dioxide will bring about toxic symptoms, such as headache, nausea and (when concentrations above 15 per cent are employed too long) convulsions. It should also be noted that carbon dioxide is a powerful cardiac whip; it produces hypertension and excessive diaphoresis due to its action as a central vasoconstrictor and a peripheral vasodilator.

Many cases of intractable hiccup that are resistant to 5 per cent carbon dioxide inhalation may be successfully treated with concentrations of 10 to 15 per cent carbon dioxide when employed up to the point of loss of consciousness. The cessation of hiccup appears related to a central effect on the brain rather than to sustained pulmonary ventilation. In cases of depressed respiration due to morphine or barbiturate poisoning, carbon monoxide is not indicated, since the carbon dioxide content of the blood is already high. This also applies to atelectasis of the lungs of the newborn.

ADMINISTRATION OF DRUGS BY INHALATION

NEBULIZATION OF BRONCHODILATOR AND ANTIBIOTIC AEROSOLS

The purpose of inhaling nebulized solutions is to deposit on the respiratory passageway and in the alveoli small droplets of substances suspended in air. The size of the particles in therapeutic aerosols exercises a critical effect on the site of deposition and absorption from the respiratory tract. Particles of small size, 0.3 to 0.8 micron in radius, pass readily through the tracheobronchial tree into the alveoli, where varying proportions, from 60 to 70 per cent, are absorbed, depending on the complex nature of the substance. Particles of relatively large size, more than 10 microns in radius, are mostly precipitated on the pharynx, larynx, trachea and larger bronchi.

The determination of the optimal particle mass for therapeutic administration depends on the location where deposition is desired and on the therapeutic substance employed. Thus, in the treatment of bronchospasm it is desirable to use a nebulin of bronchodilator solution of relatively small particle size (1 to 3 microns in radius) in order to obtain both local application to the smaller bronchi and absorption from the alveoli into the blood stream. Similarly, it is desirable to avoid the use of a vasoconstricting nebulin of large particle size in order to prevent useless deposition of drug and irritation of the larynx and trachea.

In the treatment of bronchopulmonary infections with penicillin and other antibiotic aerosols, deposition of the drug on the surface of the bronchial mucous membrane as well as absorption from the alveoli into the blood stream are accomplished by inhalation of mists of relatively small particle size, 1 to 3 microns in radius. Although maximum alveolar absorption takes place with smaller particles, 0.4 to 0.8 micron in radius, the time required for administration of mists of such small particle size is considerably prolonged with the nebulizers now in use. When treatment of nasopharyngeal and sinus infections is intended, use of an antibiotic aerosol of larger particle size appears to be desirable in order to obtain greater deposition of the drug in the nasopharynx and, with use of intermittent negative pressure, in the sinus cavities.

Treatment with nebulized bronchodilator solutions in bronchial asthma and pulmonary emphysema is conveniently carried out by the hand bulb nebulizer with 1:100 epinephrine solution, 2.25 per cent racemic epinephrine or arterenol (isopropyl epinephrine). Continuous nebulization of epinephrine and related substances, as well as chemotherapeutic substances such as the sulfonamide drugs and glucosulfone sodium (promin®), may be maintained with air from a pressure pump and with oxygen from high pressure cylinders. The sulfonamide aerosols have been largely superseded by the newer antibiotic drugs, especially penicillin and streptomycin, because of their greater clinical effectiveness. Streptomycin aerosol has been used in the treatment of bronchial and laryngeal tuberculosis, in conjunction with parenteral administration of streptomycin.

The introduction of penicillin into the nasal accessory sinuses is accomplished by the development of intermittent negative pressure in the nasal passages during the nebulization of penicillin aerosol in concentrated solutions, such as 50,000 to 100,000 units per cubic centimeter.

Inhalation of micronized or powdered penicillin and powdered streptomycin, recently introduced as a simple method of topical application, requires further study to appraise its value, but it appears at present to be less effective and more wasteful of drug than penicillin or streptomycin aerosol in the treatment of bronchopulmonary infections.

METHODS OF ADMINISTERING PENICILLIN AEROSOL

The administration of penicillin aerosol calls for an appropriate nebulizer and a source of air or oxygen under pressure. For the cooperative patient oral inhalation is employed. A glass Y tube is inserted in the rubber tubing between the nebulizer and the oxygen regulator; the finger is placed over the open end to close it during inspiration and removed during expiration. A mouthpiece attachment and a rebreathing bag may be used if it is desired that the patient reinhale some of the penicillin from the expired air; this arrangement also prevents spilling of the penicillin solution into the mouth. When a mask is employed a demand valve may be connected to the nebulizer, by which penicillin aerosol is produced only during the inspiratory cycle through a slight drop in pressure actuating the demand valve. A hood or tent is employed for simultaneous administration of penicillin and oxygen in dyspneic patients. The dosage of drug commonly used is 50,000 to 200,000 units of penicillin dissolved in 1 to 2 cc. of saline solution or distilled water.

An important detail of technic is to use one or two rinses in the nebulizer after the penicillin solution has been nebulized, since without rinses 40 per cent of the drug remains in the nebulizer in concentrated form. The rinse solution may be distilled water, saline solution, vasoconstricting and bronchodilating solutions, such as 1 per cent phenylephrine hydrochloride, 1 per cent racemic epinephrine or 1 per cent ephedrine, or benzalkonium chloride 1:1,000.

APPARATUS FOR USE OF ANTIBIOTIC AEROSOLS IN SINUSITIS

The nebulizer used for administration of penicillin aerosol in the treatment of infectious sinusitis should preferably be one which produces particles of relatively large size, such as a nebulizer of the Vaponefrin® type from which the baffle has been removed and in which the diameter of the jet has been lengthened. A greater deposition of penicillin particles in the nasal passages and perhaps a larger concentration in the accessory sinus cavities may then be provided by the use of alternating positive and negative pressure. It should be emphasized, however, that for the treatment of bronchiectasis an aerosol with a relatively small particle size, which is produced by the standard Vaponefrin,® DeVilbiss or S.P.S. nebulizer, is preferable. The baffleless nebulizer, used only for sinus and nasal infections, has the advantage of swift production of a coarse mist with the hand bulb, 1 cc. being nebulized in five minutes.

A single nose piece with a small glass trap attached to the nebulizer to contain secretions is generally employed for the treatment of sinusitis. The patient breathes through the open mouth as the mist is nebulized into the nasal passages by air or by oxygen. An oxygen flow of 5 to 8 liters per minute is employed. Negative pressure may be produced by a Venturi tube connected to the nebulizer or, in the simpler apparatus, by a hand bulb. When one uses the Venturi tube, one must close the open end with the thumb; this forces oxygen or air to pass through the nebulizer and form the aerosol. When the thumb is removed from the open end of the tube and the patient swallows, a negative pressure is created in the nasal passages and

in the antrums. When suction in the nose is felt by the patient, the thumb is promptly placed again on the Venturi tube, to direct the aerosol into the nasal passage.

The pressure required may be generated by high pressure oxygen cylinders, by a motor pump, an automobile foot pump, a hand operated fire pump or a hand bulb. The dose of penicillin which is frequently used is 50,000 to 200,000 units dissolved in 1 to 2 cc. of saline solution, or 1 per cent phenylephrine hydrochloride solution or boiled water. The Venturi tube and the nebulizer should be washed every day or two; the nose pieces should be washed after each treatment.

The Hand Bulb Method of Producing Negative Pressure.—The nebulizer may be used with a hand bulb instead of the Venturi tube to produce negative pressure. Positive pressure produced by compression of the rubber bulb forms the mist, and negative pressure is developed when the bulb expands. The patient inserts the single glass nose piece into the nostril, compresses the hand bulb to produce the aerosol, then closes the other nostril with the finger, and swallows as the bulb expands, producing a negative or suction effect in the nose. When the experience of negative pressure is noted, the bulb is again compressed, producing an aerosol of penicillin in the nasal passages. The advantage of the bulb technic of producing negative pressure lies not only in its simplicity but also in the fact that the penicillin mist enters the nasal passages during the latter part of the phase of negative pressure, as the bulb expands. Since 1 cc. of solution may be nebulized by the hand bulb in five to ten minutes when the large jet, baffleless nebulizer is employed, this apparatus lends itself to home treatment, without the use of oxygen or a motor-driven pump. More effort is naturally required for the hand bulb method than with the use of a source of pressure, such as a cylinder of oxygen or an air pump, or hand or foot pumps. However, in each instance a negative pressure of 50 to 60 mm. of mercury may be attained in the nasal passages and transmitted to the accessory sinuses.

CLINICAL ILLUSTRATIONS OF NEED FOR INSTRUCTION

The lack of adequate teaching of inhalational therapy was recently manifested in a clinic on inhalational and physiologic therapy of respiratory disease. Four problems in treatment were presented for which physiologically directed therapy was indicated.

A statement of each case history was presented, with a request for a correct answer, to a group of forty physicians interested in diseases of the chest. Only four of them had answers that would aid the patients.

CASE 1.—A patient with pulmonary emphysema was short of breath as a result of upper respiratory infection. She was placed in an oxygen tent at a flow of 7 liters per minute, with the canopy carefully tucked in on all sides, and with a temperature and humidity within the normal range. A concentration of 60 per cent oxygen was obtained one hour later. However, the patient revealed increasing shortness of breath which was relieved promptly after the tent was removed. The previously existing dyspnea returned to the same degree present before treatment with oxygen. What was the cause of the increased dyspnea in 60 per cent oxygen?

CASE 2.—A patient with bronchial asthma was treated in a B-L-B mask at a flow of 4 liters per minute to provide a concentration of 40 per cent oxygen, according to the literature that came with the mask apparatus. Within fifteen minutes there was a pronounced increase in the dyspnea of the patient which was relieved after the mask was removed. What was wrong in the handling of this patient?

CASE 3.—A patient with hypertensive vascular disease and coronary arteriosclerosis had acute widespread pulmonary edema at night. After treatment with a Meter mask, providing an expiratory positive pressure of 5 cm. of water, the lungs were clear at the end of one hour. The mask was removed, but within thirty minutes there was a return of pulmonary edema. What form of treatment was then indicated?

CASE 4.—A patient manifested acute widespread edema of a lung after six days of continuous inhalation of 95 to 100 per cent oxygen in a B-L-B mask. The pulse rate was 150; the respiratory rate was 70. An expiratory positive pressure mask, with a pressure on expiration of 5 cm., was used and the oxygen concentration was lowered to 60 per cent. A decided increase in cyanosis took place. What should the subsequent program of treatment have been?

Clinical situations of this type are common, and, unfortunately, the inability to prescribe proper treatment is revealed not only among general practitioners but among specialists in diseases of the chest.

In case 1 increased dyspnea was due to a carbon dioxide concentration of 2.5 per cent, which resulted from the low rate of flow of oxygen (7 liters per minute) and an inadequate washing out of carbon dioxide. The patient who eliminates 250 cc. of carbon dioxide per breath must have this diluted in 2,500 cc. of air plus oxygen in order to lower the concentration to 1 per cent. A flow of not less than 10 liters per minute, maintaining an oxygen concentration of 50 per cent, must be used in order to bring about a dilution of carbon dioxide and thus prevent increased pulmonary ventilation and aggravation of dyspnea. To maintain a concentration of 60 per cent oxygen requires a flow of 12 to 14 liters per minute.

In case 2 a flow of 4 liters per minute in the B-L-B mask was insufficient to wash out carbon dioxide; the concentration of carbon dioxide in the mask was 2.5 per cent. In addition, the collapse of the bag during inspiration made it necessary for the patient to suck air through the sponge rubber disks, which required increased inspiratory effort. The negative pressure within the mask when the sponge rubber disks are new may be from 1 to 1.5 cm. of water, but when they are clogged with dust the resistance is even higher. The patient with bronchial asthma should have a flow in a B-L-B mask of not less than 7 liters per minute in order to wash out the major part of the carbon dioxide and to prevent collapse of the bag during inspiration. (In the injector type meter mask the mixture of oxygen and air takes place at the regulator as a result of the pressure of oxygen itself in the injector.)

The patient with pulmonary edema in heart disease (case 3) was treated again with a Meter mask providing an expiratory positive pressure of 5 cm. of water; when the moisture had cleared, pressure was gradually lowered from 5 to 4 cm., 4 to 3, 3 to 2 and 2 to 1, i. e., a lowering of 1 cm. at half hour intervals. In these circumstances the heart was offered a gradually increased volume of blood, so that left ventricular failure was not induced by sudden entrance of a large amount of blood.

In case 4 treatment was continued with 60 per cent oxygen, since this concentration is not irritating to the lungs. Despite the temporarily increased cyanosis, the patient was decidedly improved; at the end of thirty-six hours the pulmonary edema had subsided. The pressure was gradually lowered, and the patient ultimately recovered.

These cases are cited in order to emphasize the lack of knowledge on the part of physicians concerning the functioning of the apparatus that is commonly employed, as well as an incomplete understanding of the pathologic physiology of the conditions themselves.

NEED FOR TRAINED PERSONNEL

The advantages of theoretic knowledge of the physiology and pathology of respiratory disorders are not transmitted to the patient unless the technics are skillfully administered. Because of the complexity and diversity of modern apparatus, technicians must be properly trained and supervised. In New York City the Board of Health conducts examinations for licensure of technicians in inhalational therapy. Although at present licensure applies solely to those in the business of supplying inhalational therapy services and proprietary hospitals, it provides an opportunity for extension to hospital personnel. Hospitals have not generally considered it feasible to supply trained technicians for the administration of inhalational therapy; it is usually relegated to a changing intern staff or to nurses and orderlies who as often as not have not had proper instruction.

The fact that few medical schools and hospitals provide instruction in inhalational therapy is another factor responsible for a lack of competent supervision of this type of treatment of conditions due to impaired respiratory function. Frequently the trained technician is more familiar with the procedures than is the physician, a situation which in all probability will continue until adequate teaching of inhalational therapy is undertaken by medical schools and hospitals.

Still another factor appears to be the unwillingness of physicians interested in respiratory physiology or in diseases of the chest to assume the directorship of departments of inhalational therapy in the absence of full time trained technical assistants. Physicians who refuse such assignments would appear to be abundantly justified, since they themselves would be called on either to carry out in person time-consuming procedures or else to take responsibility for improper practice by poorly trained hospital personnel.

In some hospitals the anesthesiologist has been placed in charge of the therapeutic use of gases and pressures because of his familiarity with the inhalation of anesthetic agents. Unfortunately, clinical problems at times arise in disturbances of respiratory function in which he is not qualified as a consultant. To establish him in the role of glorified technician in charge of equipment and technic is of advantage neither to him nor to the hospital. If hospitals were required to provide trained inhalational therapy technicians, the physician specializing in respiratory disease might be interested in heading such a department, conducting studies on those clinical entities characterized by impaired respiratory function and providing the hospital clinic with consultative services, when desired; such services might prove to be of value to those of his colleagues less well informed concerning the physiologic and technical problems involved.

SUMMARY

The purpose of inhalational therapy may be broadly described as the attempt to restore normal function to the respiratory system. Impairment of respiratory function ultimately manifests itself in a lack of oxygen in the tissues. At times this may be counteracted by simple inhalation of an oxygen-enriched atmosphere. In recent years, however, the recognition of more complex pathophysiologic changes in the organs of breathing has stimulated the development of various means of controlling pressure as well as the therapeutic use of gases.

Alleviation of anoxia is frequently of crucial importance in such conditions as cardiac failure, coronary artery disease, asthma, pulmonary emphysema, atelectasis of the lungs, pneumonia, pulmonary edema and cerebral thrombosis. A proper understanding of the technics of modern procedures in inhalational therapy is essential if the value of this type of physiologically directed therapy is actually to be brought to the bedside. An attempt has been made herein to formulate the methods now in use in order to promote a more effective employment of inhalational therapy.

Although no emergency is more critical in clinical medicine than an interruption in the lifeline of oxygen, the failure to teach inhalational therapy in medical schools is almost universal.

The lack of skilled technicians in many hospitals is responsible for inexpert management of the methods of treatment, which are generally relegated to a changing intern staff, nurses or orderlies.

Physicians interested in respiratory physiology or in diseases of the chest would seem to be the most suitable as heads of departments of inhalational therapy in hospitals because of the complexity of the problems in internal medicine for which consultative services are needed. However, without specially qualified technical assistants the director would find himself carrying out procedures of a burdensome and time-consuming nature, or, equally unfortunately, delegating serious responsibility to unskilled personnel.

Registration of technicians and technician supervisors who have been qualified by written and oral examinations, as already established in New York City by the Board of Health, constitutes the beginning of a program whereby hospitals may acquire an expert inhalational therapy service. This type of service is of crucial importance in the management of the many clinical entities characterized by impairment of respiratory function.

Council on Foods and Nutrition

DEFICIENCIES OF THE FAT-SOLUBLE VITAMINS

JOHN B. YOUMANS, M.D.
Nashville, Tenn.

This paper was prepared at the request of the Council and is one of a series appearing in THE JOURNAL. *In the near future the entire series will appear in book form as the Council's Handbook of Nutrition.*

JAMES R. WILSON, M.D., *Secretary.*

VITAMIN A

In addition to the general limiting effect on growth common to all nutrients, vitamin A seems to affect almost exclusively the mechanism of the adaptation of vision to dim light (dark adaptation) and the health and integrity of the epithelium. The functional and structural changes resulting from a deficiency of this vitamin constitute the manifestations of the deficiency disease.

Dark Adaptation.—The adaptation of vision to dim light, principally a function of the retinal rods, requires an adequate supply of vitamin A (vitamin A_1). The process depends on the presence of an adequate amount of visual purple (rhodopsin). Vitamin A with a protein forms visual purple. Visual purple, or rhodopsin, is reversibly broken down in bright light to retinene,

From the School of Medicine, Vanderbilt University, Nashville.

which in turn is reconverted to vitamin A_1 by a reaction involving reduced cozymase as a co-enzyme. Recent studies indicate a complicated process possibly involving two other vitamins, nicotinic acid and vitamin E, as well as proteins.[1] The continuous process of breakdown and regeneration, while obviously a reversible process, is not completely so and is accompanied with some loss of vitamin A, requiring a supply for replacement. Without an adequate supply, the formation of visual purple fails and poor dark adaptation (night blindness) results.

Poor dark adaptation (night blindness, or nyctalopia) has been known for centuries in circumstances now known to be related to deficient intakes of vitamin A. It occurs also under conditions interfering with the absorption, storage and utilization of vitamin A and carotene or the conversion of the latter to vitamin A. Such conditions include gastrointestinal disease, sprue and disease of the liver.

Slight night blindness is not recognizable except by instrumental means, even by the subject. Mild complaints include difficulty in reading, sewing or detecting objects in dim light and stumbling in the dark, particularly on sudden changes from bright to dark. There may also be undue sensitivity to sudden bright light. In severe cases the subject is so blind as to be incapacitated in dim light.

Epithelium.—Although vitamin A deficiency affects the epithelium in many sites, certain places are for one reason or another of greater clinical importance than others. They are the eyes, the skin, the upper parts of the respiratory passages, the bronchi and perhaps the genitourinary tract. These are of particular importance, either because their location makes them readily observed or because the symptoms they produce are particularly important.

Eyes: The changes in the epithelium of the eye involve particularly the scleras, the corneas and the tear glands and ducts. The other glands and the conjunctivas are involved to a lesser extent. Perhaps the earliest noticeable change is functional, decreased tearing, although it is possible that this is preceded by a brief stage of increased lacrimation. The characteristic "conjunctivitis" of vitamin A deficiency, however, is a dry conjunctivitis. This is accompanied with itching and burning and, perhaps, some redness of the conjunctivas. Follicular conjunctivitis and granular lids have been reported as a result of the deficiency; this stage has been called prexerosis. Another early change is cornification of the epithelium of the corneas and scleras, particularly the latter. This can be detected in stained smears obtained from corneal or scleral scrapings, the epithelial cells showing the characteristic staining reactions and structural changes of keratinization or cornification. As the disease progresses, the metaplasia, cornification and desquamation of the ocular epithelium increases. Secretion of tears ceases. On the scleras, there is a piling up of epithelium to form localized "spots," areas of thickening, with a decreased translucency. When fully developed they may become Bitot's spots, silvery or pearly raised, usually triangular, areas, with the base toward the cornea and, as a rule, lateral to the cornea on the equator of the eye. There may be a pigmented background. The scleras take on a greasy appearance and wrinkle easily, at the same time becoming generally more opaque and lusterless. There is edema of the cornea and infiltration with leukocytes, at first in localized areas, later becoming diffuse and involving the entire cornea, the latter change often appearing precipitously. At about this point, or somewhat before, the stage known as xerophthalmia or keratomalacia is present, and progression of the disease is often followed by secondary infection (corynebacterium xerose is a common invader), panophthalmitis, hypopyon and often loss of the eye. Vision is impaired from the beginning of corneal keratinization and clouding. Microscopically, there is metaplasia followed by atrophy and desquamation of the epithelium of the tear glands and ducts, as well as the cornification of the scleral and corneal epithelium.

In addition to these changes, Kruse [2] has described what he considers still earlier or milder changes, mainly in the subepithelium, detectable only with magnification and proper illumination (slit lamp and suitable microscope). Others,[3] however, believe these to be senile and presenile changes or the effect of physical or other irritants, such as wind and dust, rather than the result of vitamin A deficiency. An important criticism of Kruse's theory is the failure of the lesions to clear, despite administration of large doses of vitamin A over long periods. In animals [4] the response is rapid and complete. It is true that the lesions may be more chronic in man, but it is difficult to accept failure of cure in so slight a lesion as consistent with Kruse's hypothesis. Elsewhere the repair, microscopically as well as grossly, is relatively rapid. In rabbits the corneal epithelium, corneal nerve fibers and retina are not affected, nor does corneal vascularization or infiltration occur. In subjects with true xerosis or xerophthalmia, the level of vitamin A in the blood is usually low,[5] as is true experimentally.

Recovery following treatment may be incomplete, and scars are left if the damage has passed beyond the reversible stage. This occurs fairly early in the case of the cornea, and corneal scars are not uncommon. Otherwise, the eye returns to normal.

Upper Part of the Respiratory Tract: Changes similar to those in the conjunctiva and the lacrimal glands occur in the mucosa of the upper part of the respiratory tract, notably in the sinuses and nares. The eustachian tubes and salivary glands and ducts are similarly involved. The nares are of particular importance because they provide a handy source of epithelial scrapings, which may be of some help in diagnosis, at least in infants. Such changes may favor the occurrence or at least the persistence of localized infections. In the mouth and throat these same changes occur, but the normal degree of cornification at these sites makes them of little practical interest. Despite some speculation on the relation of these changes and vitamin A deficiency to buccal leukoplakia, no definite relationship has been established. However, the presence of characteristic alterations in the salivary glands and ducts is easily shown.

Bronchi: The stratification, cornification and desquamation of the mucosal epithelium of the bronchi, bronchioles and bronchial glands is of particular clinical importance because of their relation to atelectasis and pneumonia in infants. The process is said to be the

1. Wald, G.: The Enzymatic Reduction of the Retinenes to the Vitamins A, Science **109**: 482, 1949.

2. Kruse, H. D.: The Detection of Ocular Changes in Avitaminosis A, Pub. Health Rep. **56**: 1301, 1941.

3. Berliner, M. L.: Regarding the Early Detection of Avitaminosis A by Gross or Biomicroscopic Examination of the Conjunctiva, Am. J. Ophth. **25**: 302, 1942.

4. Mann, I.; Pirie, A.; Tansley, K., and Wood, C.: Some Effects of Vitamin A Deficiency on the Eye of the Rabbit, Am. J. Ophth. **28**: 801, 1946.

5. DeHaas, J. H., and Meulemans, O.: Vitamin A and Carotenoids in Blood Deficiencies in Children Suffering from Xerophthalmia, Lancet **1**: 1110, 1938.

most common mechanism of death in infants dying of vitamin A deficiency.[6] With the epithelial metaplasia and atrophy there is, of course, loss of cilia and decrease or cessation of bronchial secretions. What part these changes may play in chronic disease, particularly in chronic infections of the bronchi, is not well established.

Genitourinary Tract: Metaplasia of the epithelium, followed by cornification, desquamation and replacement with stratified epithelium, undoubtedly occurs in the genitourinary tract. It is questionable whether or not the leukoplakia in this area is the result of vitamin A deficiency.[7]

In the renal pelvis and in the bladder such changes have been alleged to provide a nidus of desquamated epithelium about which the desposition of mineral salts form calculi. A noninfectious vaginitis, especially in elderly women, has been attributed to the same cause.[8] Neither has been clearly established clinically. Similar changes in the epithelium of other organs, such as the pancreas, have been suspected, but attempts to link vitamin A deficiency with such conditions as fibrocystic disease of the pancreas have failed. Absence and defective formation of dentin and enamel of the teeth occur, with resulting deformities of the teeth.

Skin: Much has been written and considerable uncertainty and difference of opinion has arisen over the question of changes in the skin in vitamin A deficiencies. In part this is a reflection of the general lack of knowledge concerning cutaneous lesions in any of the deficiency states. As Wolbach points out,[9] no one has as yet been able to correlate such lesions with known functions of the skin or "the normal morphologic sequences of the epidermis and its appendages."

There can be little doubt that a characteristic dermatitis occurs as a result of vitamin A deficiency, as described in the classic papers of Frazier and Hu [10] and Loewenthal.[11] The differences of opinion and the uncertainty have occurred in part because of the designation by some writers of minor abnormalities of the skin as characteristic of vitamin A deficiency. Such changes, dryness, for example, which, occurring in vitamin A deficiency, is nonspecific, occur from many other causes. Their presence, labeled as a sign of vitamin A deficiency, in circumstances clearly eliminating such as a cause, has been confusing. In part such confusion has resulted from a lack of proper knowledge and understanding of various diseases and abnormalities of the skin on the part of some observers. As an example, ichthyosis, a congenital disorder of the skin unrelated to vitamin A, is confused by some with the dermatosis resulting from vitamin A deficiency.

The typical, characteristic lesion of the skin in vitamin A deficiency is the dry, horny, perifollicular, hyperkeratotic papule. Microscopically, the papule is seen to arise from and about the pilosebaceous follicle. The lumen and mouth of the follicle are enlarged and filled with a plug of dense, horny, cornified, desquamated epithelium arranged in concentric lamellas, often surrounding the remnant of a hair. There are varying degrees of metaplasia and keratinization of the follicular epithelium, with hyperplasia of adjacent epidermal cells and hypertrophy and hyperkeratinization of the superficial epidermis. There is a mild, irritative, inflammatory reaction of the cutis vera around the follicles, with little cellular infiltration. There are varying grades of metaplasia and atrophy of the sebaceous glands, and many may disappear. Sweat glands and ducts show similar changes. There is some increase in melanin about the follicles. In the type described as acneform the changes are similar and resemble the changes in acne without the cellular infiltration.

The papules range in size from pinhead to 5 cm. in diameter and are distributed principally on the extensor surfaces of the arms and thighs, shoulders, abdomen, back and buttocks, in frequency in the order named. The papules are conical or hemispherical and contain the central plug. When the latter is expressed, a gaping hole is left. Hairs are short, broken off or absent. There may be increased pigmentation about the papule. Infection is absent in uncomplicated cases, but pustules and furuncles may be present as a complication. In addition to these more characteristic lesions, the skin is commonly dry and rough, with a fine, branny desquamation. So-called crackling, a change resembling ichthyosis somewhat, is not, in my opinion, a significant observation. It is most often observed on the lower leg, an area infrequently involved by the papular eruption.

In this country papules of large size or extensive distribution are uncommon. The usual lesion is about the size of the papule of ordinary "gooseflesh," with which it may be confused unless one takes care to note the chilliness and strokes the area, causing the papules to disappear. Washing may lessen the eruption, a natural result, since the effect is to remove the heaped-up dead epithelium. It should not be allowed to be misleading.

In certain patients a somewhat different lesion appears to be the result of vitamin A deficiency.[12] This is an acne-like eruption with dull red, flat or slightly conical, discrete papules of about the usual size of the acne papule. The individual lesions often simulate a pustule, but the whitish top, when pierced or removed, proves to be a thin scale with a raw surface but no pus underneath. Significant features are the occurrence of the lesion after the patient is beyond the ordinary age at which acne occurs and a distribution of the lesions over the anterolateral surface of the arms and back, with few if any on the face or abdomen. They may be found on the thighs and buttocks. The skin is not dry or rough, and the lesions seem more common in those who bathe frequently. An association of vitamin A deficiency with true acne has been suspected but has not been established.[13] There is evidence to indicate that comedos may have a similar relationship, at least in part.[14]

The dermatosis of vitamin A deficiency is uncommon in children before puberty, which has been related by Frazier and his associates [15] to changes in the sebaceous glands and hair which occur at that time. The varia-

6. Blackfan, K. D., and Wolbach, S. B.: Vitamin A Deficiency in Infants: Clinical and Pathological Study, J. Pediat. **3**: 679, 1933.

7. Patch, F. S.: Epithelial Metaplasia of the Urinary Tract, J. A. M. A. **136**: 824 (March 20) 1948.

8. Simpson, J. W., and Mason, K. E.: A New Concept of Senile Vaginitis, Am. J. Obst. & Gynec. **32**: 125, 1936.

9. Wolbach, S. B.: Pathology in Relation to Nutritional Research, Nutrition Rev. **3**: 193, 1945.

10. Frazier, C. N., and Hu, C. K.: Cutaneous Lesions Associated with a Deficiency of Vitamin A in Man, Arch. Int. Med. **48**: 507, 1931.

11. Loewenthal, L. J. A.: A New Cutaneous Manifestation in the Syndrome of Vitamin A Deficiency, Arch. Dermat. & Syph. **28**: 700 (Nov.) 1933.

12. Youmans, J. B., and Corlette, M. B.: Specific Eruptions of the Skin Due to Deficiency of Vitamin A, Tr. A. Am. Physicians **52**: 49, 1937; Specific Dermatoses Due to Vitamin A Deficiency, Am. J. M. Sc. **195**: 644, 1938.

13. Lynch, F. W., and Cook, C. D.: Acne Vulgaris Treated with Vitamin A, Arch. Dermat. & Syph. **55**: 355 (March) 1947. Straumfjord, J. V.: Vitamin A: Its Effect on Acne; A Study of 100 Patients, Northwest Med. **42**: 219, 1943.

14. Hohmann, W. J., and Beening, G. W.: Epidemic of Comedones and Vitamin A Deficiency, Nederl. tidjschr. v. geneesk. **91**: 1465, 1947.

15. Frazier, C. N., and Hu, C. K.: Nature and Distribution According to Age of Cutaneous Manifestations of Vitamin A Deficiency: Study of 207 Cases, Arch. Dermat. & Syph. **33**: 825 (May) 1936. Frazier, C. N.; Hu, C. K., and Chu, F.: Variations in the Cutaneous Manifestations of Vitamin A Deficiency from Infancy to Puberty, ibid. **48**: 1 (July) 1943.

bility of vitamin needs at different periods of growth and development under the influence of endocrine functions and the greater demands at certain periods are important in this regard.

It must be emphasized that the specificity of the skin lesions has not been established, and doubt has been expressed of their relationship to vitamin A. The observations and conclusions of Sullivan and Evans [16] are frequently referred to in this respect and are of particular interest because they represent what I believe is a misunderstanding of the nature of the lesions and a misinterpretation of experimental observations. These workers question the relation of vitamin A to the dermatosis just described on the following basis: The pathogenesis of the epithelial lesions of vitamin A deficiency is assumed to be atrophy followed by metaplastic epithelial hyperkeratinization. The skin is already keratinized; therefore, how can such changes occur? Sullivan and Evans support their conclusions by studies in rats: dermal lesions failed to develop in rats on a diet deficient in vitamin A, but, when a deficiency of B vitamins was added, a thin, atrophic skin, followed later by some keratinization of the hair follicles, did develop. Such an argument misses the essential point, as it is often missed clinically, that the lesion in man is primarily a lesion of the follicles and sebaceous sweat glands. The papule is a perifollicular papule. The epithelium of the hair follicles, sweat glands and sebaceous glands is not normally keratinized; it becomes so. The changes in the horny layer, while present, are not great or especially characteristic.

The question of the relation of vitamin C to the dermatosis commonly attributed to vitamin A deficiency is more difficult. Lesions of the skin, apparently identical, except for hemorrhage, with those attributed to vitamin A deficiency, have frequently been described in cases of scurvy.[17] This has generally been interpreted as indicating the presence of a deficiency of vitamin A and C, though some writers have considered it a manifestation of vitamin C deficiency alone. This view has been strengthened and the question of the relation of vitamin A to the dermatosis considerably clouded by the development of such an eruption in human subjects with experimentally induced scurvy (hypovitaminosis C).[18] In the latter cases, however, as in the naturally occurring cases, the papules have been hemorrhagic except in the earliest stages. In typical cases of what has been thought to have been vitamin A dermatosis there has been no hemorrhage.

Perhaps the solution of this problem lies in recent observations on vitamin A deficient rats.[19] These animals exhibited signs of scurvy which were relieved with massive doses of ascorbic acid. Previous workers had shown lowered levels of ascorbic acid in blood and tissue in experimental animals rendered deficient in vitamin A.[20] If the possibility be accepted that a deficiency of one vitamin may cause at least an effective deficiency of another, as in this instance, then a deficiency of vitamin C might lead to a deficiency of vitamin A, with the development of the characteristic dermatosis, which, in such circumstances, might have the added picture of hemorrhage. In any event, it is my opinion that in many instances the dermatosis described is the result, directly or indirectly, of vitamin A deficiency and should be so treated. It cannot, however, be considered specific or pathognomonic at present. As in all but pathognomonic lesions, all factors must be taken into consideration in any given case. The presence of one or two papules does not warrant a diagnosis; neither does dryness and desquamation. The lesions are falsely exaggerated by cold (gooseflesh). Naturally, the rash can be improved by a bath, a fact sometimes cited as evidence against its being the result of vitamin A deficiency. The excess cornified epithelium is removed mechanically. Finally, and unfortunately, confusion has arisen because of the time lag in both the appearance and disappearance of the eruption in relation to blood levels of vitamin A, dark adaptation tests and treatment with vitamin A.

It must be remembered that considerable time is required for the structural changes in the skin to occur, both in the development of the lesion and in its restoration to normal, while changes in the concentration of vitamin A in the blood (particularly an increase) and in dark adaptation can occur many times more rapidly. Hence, direct correlation with changes in the skin at any one time may fail.

A few other lesions, notably corns and calluses, have been attributed to vitamin A deficiency.[21] Though such a relationship has not been established, a fairly good case, theoretically, could be made for it. Such lesions consist essentially of an increased local cornification, which might occur on the basis of a local, relative deficiency induced by pressure ischemia or some similar cause. In relating any such possibility to treatment, full consideration must be given to the long time needed to produce significant changes.

Diagnosis.—Recognition or detection of vitamin A deficiency rests on the diagnostic triad of history, physical examination and laboratory tests. The history includes inquiry not only into the symptoms but into the dietary (or other) intake of vitamin A. The symptoms are usually conjunctivitis, asthenopia, dryness of the eyes, difficulty in vision (even night blindness) and the eruption. In more advanced cases there are, of course, severe ocular symptoms. Children fail to gain weight, which for them is probably the first symptom, and, if pulmonary complications develop, they exhibit the usual symptoms of such disease. Examination reveals the gross changes in the eyes, mucous membranes and skin previously described. In advanced disease night blindness is detected by gross testing.

There are three laboratory or special tests. A test of dark adaptation, examination of smears from epithelial surfaces for cornification of the epithelium and determination of the concentration of vitamin A and carotene in the blood.

Tests of dark adaptation with suitable adaptometer or photometer will undoubtedly detect a mild or severer grade of night blindness due to vitamin A deficiency. Vitamin A deficiency is not the only cause of night blindness, but that need not destroy the value or significance of the test if it is employed properly. The greater difficulty comes with extremely slight grades

16. Sullivan, M., and Evans, V. J.: Nutritional Dermatoses in the Rat: XI. Vitamin A Deficiency Superimposed on Vitamin B Complex Deficiency, Arch. Dermat. & Syph. **51**: 17 (Jan.) 1945.

17. Scheer, M., and Keil, H.: Follicular Lesions in Vitamin A and C Deficiencies, Arch. Dermat. & Syph. **30**: 177 (Aug.) 1934.

18. Vitamin C Requirement of Human Adults: Experimental Study of Vitamin C Deprivation in Man; A Preliminary Report by the Vitamin C Sub-Committee of the Accessory Food Factors Committee, Medical Research Council, Lancet **1**: 853, 1948.

19. Mapson, L. W., and Walker, S. E.: The Synthesis of Ascorbic Acid in the Rat Deprived of Vitamin A With and Without Addition of Chloretone, Brit. J. Nutrition **2**: 1, 1948. Jonsson, G.; Obel, A.-L., and Sjöberg, K.: Skorbut als Sekundärerscheinung bei A-Avitaminose, Ztschr. f. Vitaminforsch. **12**: 300, 1942. Mayer, J., and Kiehl, W. A.: Scorbutic Symptoms in Vitamin A Deficient Rats, Arch. Biochem. **16**: 313, 1948.

20. Sure, B.; Theis, R. M., and Harrelson, R. T.: Vitamin Interrelationship: I. Influence of Avitaminosis A on Ascorbic Acid Content of Various Tissues and Endocrines, J. Biol. Chem. **129**: 245, 1939.

21. Straumfjord, J. V.: Lesions of Vitamin A Deficiency: Thin Local Character and Chronicity, Northwest Med. **41**: 229, 1942.

of night blindness, or better still, extremely slight variations in dark adaptation detected by means of an accurate photometer. Such variations are frequently within the limits of error resulting from such factors as subjective response, learning factor, motivation and slight errors in technic. It is not surprising, therefore, that failure to correlate variations in photometric measurements with other data, such as dietary intake, levels of vitamin A in the blood and history and physical signs should have occurred. Also, regardless of diet and preceding stores of vitamin A, children who have colds and certain other minor ailments show poor adaptation promptly. Adaptation returns to normal with recovery from the illness. In selecting subjects with poor adaptation, some investigators may have selected those who were temporarily affected with minor illness. With recovery from the illness, adaptation improved irrespective of vitamin A additions. A learning factor is not involved in such circumstances. This should not be taken as an excuse for the use of inaccurate or improper instruments, but it does mean that standards should be adopted, based on careful experimental evidence, which will clearly differentiate real changes in dark adaptation. Even with this limitation, it is possible that night blindness can be detected by instrumental means earlier than otherwise, and the proper instruments should be used for this purpose. Other causes of night blindness must, of course, be eliminated before the condition can be attributed to vitamin A deficiency, but ordinarily this is easy. It should be remembered, however, that vitamin A deficiency can probably occur and manifest itself before night blindness develops, although in man night blindness can occur and be demonstrated before corneal and conjunctival changes become grossly apparent. In experimental animals the concentration of vitamin A in the retina may remain normal while that of the blood is reduced greatly and, under treatment, returns to normal before that of the blood.[8] Finally, other ocular defects, including those due to other nutritional deficiencies, may cause error.

Microscopic examination of scrapings from the nose to determine the presence of cornification of the epithelium has been recommended in the diagnosis of the condition in infants.[22] Similar examination of scrapings from the scleras and corneas has been suggested for use with adults. In my experience, the latter is neither suitable nor reliable, at least for the diagnosis of slight deficiency.[23] In the same category is the demonstration of excessive epithelium in urinary sediments or vaginal smears, although this should arouse suspicion of a possible vitamin A deficiency.

Determination of the concentration of vitamin A and carotene in the blood is useful in diagnosis and is probably the best laboratory aid. The concentrations of the two substances do not necessarily parallel each other, however. Carotene values are easily influenced by dietary intake, hepatic disease or disorders of absorption, without, of necessity, the concentration of vitamin A being affected. For this reason, the two determinations are useful in differential diagnosis of such other diseases as sprue and hepatitis. For the diagnosis of vitamin A deficiency, the vitamin A concentration is much more helpful and reliable. Low values are found in a fully developed deficiency. However, the storage of vitamin A is ordinarily great in adults, and a considerable time is needed to deplete these stores. The exact levels at which vitamin A deficiency actually exists have not been established. In part, this is due to dissimilarity of method and the failure of the various investigators to follow similar procedures. In experimental animals the concentration of vitamin A in the blood has been observed to have fallen to 10 per cent or less of normal before microscopic lesions were detected in the eyes.[8]

Several methods, nearly all of which use the Carr-Price reaction and involve the use of a photoelectric colorimeter, are available.[24] Those are probably the most practical for ordinary clinical use. A micromethod, using the measurement of ultraviolet ray absorption with a spectrophotometer, has been developed [25] and is useful when one is dealing with small amounts of blood or making mass determinations. Recently other technics have been introduced which may offer certain advantages.[26]

No final agreement has been reached on normal standards for vitamin A. There is a wide acceptance of a lower normal value for adults of 70 international units (approximately 20 micrograms) per hundred milliliters of serum or plasma. Values for infants may be lower, but an exact level cannot be stated with certainty. Some evidence suggests 20 micrograms as the lower normal value for infants.

Studies of experimental deprivation in humans [27] showed clearly that no symptoms or signs appeared until the concentration in the serum dropped below 40 international units (approximately 12 micrograms) per hundred milliliters. The earliest manifestation was night blindness detected by instrumental methods.

Accordingly, it would appear that values below 40 international units per hundred milliliters of serum or plasma may be associated with clinical evidence of deficiency but must be interpreted in the light of other evidence. The lowest value found by Lewis and his associates [28] in what they considered normal infants was 45 international units per hundred milliliters, and this value has been suggested as a low normal level. Values below this were associated with deficient diets and disorders of fat absorption. Children 6 to 12 years old had concentrations similar to those of adults. Conservatism would require that the concentration be extremely low before it is considered strong evidence of an actual deficiency, especially in the absence of other evidence.

As indicated, carotene values are so much affected by intake and other factors not necessarily related to a deficiency of vitamin A that they are of much less use in the diagnosis of this condition. The usual figures in normal, healthy adults appear to be between 60 and 200 micrograms per hundred milliliters. Low

22. Sweet, L. K., and K'Ang, H. J.: Clinical and Anatomic Study of Avitaminosis A Among the Chinese, Am. J. Dis. Child. **50**: 699 (Sept.) 1935.

23. Youmans, J. B.; Corlette, M. B.; Corlette, M. G., and Frank, H.: Inadequacy of Conjunctival Smear in the Diagnosis of Slight Vitamin A Deficiency in Adults, J. Lab. & Clin. Med. **25**: 665, 1938.

24. Clausen, S. W., and McCord, A. B.: The Carotenoids and Vitamin A of the Blood, J. Pediat. **13**: 635, 1938. Kimble, M. S.: The Photocolorimetric Determination of Vitamin A and Carotene in Human Plasma, J. Lab. & Clin. Med. **24**: 1055, 1939. May, C. D.; Blackfan, K. D.; McCreary, J. F., and Allen, F. H., Jr.: Clinical Studies of Vitamin A in Infants and in Children, Am. J. Dis. Child. **59**: 1167 (June) 1940. Dann, W. J., and Evelyn, K. A.: The Determination of Vitamin A with the Photoelectric Colorimeter, Biochem. J. **32**: 1008, 1938. Josephs, H. W.: Studies in Vitamin A: Relation of Vitamin A and Carotene to Serum Lipids, Bull. Johns Hopkins Hosp. **65**: 112, 1939.

25. Bessey, O. A.; Lowry, O. H.; Brock, M. J., and Lopez, J. A.: The Determination of Vitamin A and Carotene in Small Quantities of Blood Serum, J. Biol. Chem. **166**: 177, 1946.

26. Sobel, A. E., and Snow, S. D.: The Estimation of Serum Vitamin A with Activated Glycerol Dichlorohydrin, J. Biol. Chem. **171**: 617, 1947.

27. Vitamin A Deficiency and the Requirements of Human Adults: Report of the Vitamin A Sub-Committee of the Accessory Food Factors Committee, Nature **156**: 11, 1945.

28. Lewis, J. M.; Bodansky, O., and Haig, C.: Level of Vitamin A in Blood as Index of Vitamin A Deficiency in Infants and in Children, Am. J. Dis. Child. **62**: 1129 (Dec.) 1941.

values (below 30 micrograms in adults) are usually associated with either a low intake or defective intestinal absorption. In infants, the serum or plasma carotene level is usually zero or approximately that until quantities of green and yellow vegetables and fruits or other carotene-containing foods are eaten.

Temporary fluctuations in the concentration of vitamin A occur as an effect of the ingestion of alcohol or fever, but ordinary meals do not affect the concentration, and it is not necessary that the blood be tested with the patient in the fasting state. A rise occurs after the administration of large doses of the vitamin, and a tolerance test may be used such as that proposed by Ruch, Brunsting and Osterberg.[29] Such a test is also used in the diagnosis of other diseases, especially those affecting the absorption of fat.

For the reasons stated, correlation between blood levels and other aspects of vitamin A nutrition and deficiency need not occur and may not be observed when they are present unless due allowance is made for the time-lag factor.

Incidence.—The incidence of actual vitamin A deficiency is unknown. Xerophthalmia and keratomalacia are certainly rare in adults in this country. They are not common in children. The same may be said of frank night blindness. What the incidence of mild deficiency—as represented by slight (detectable only with instruments) grades of night blindness, slight dermatosis or debatable changes in the scleras may be—depends on one's interpretation and evaluation of such signs. The strikingly high incidence, based on adaptometer readings, which was reported so frequently a few years ago seems scarcely credible. In a survey of a general population,[30] only 11 of 450 subjects tested had values for serum vitamin A below 30 international units per hundred milliliters (0 to 29). Of these, 8 were children (under 15 years of age), although these values are probably significant even for them. Forty-five, or 18 per cent, of the adults (21 years of age or over) had less than 70 units. Of this latter group, 33 per cent had greater or lesser impairment of dark adaptation, as measured with an adaptometer (Hecht). In the total population of approximately 1,200 persons, only some 35, or about 3 per cent, had a dermatosis. This dermatosis, however, was found in about one fifth of the 40 white male subjects of the age group 16 to 20.

In a survey of the blood levels of vitamin A in school children in New York State, Bessey and Lowry [31] found 0 to 1 per cent of those tested in eight different schools with values below 70 international units per hundred milliliters. From 1 to 10 per cent had values below 105 international units, which the authors classed as "fair." The incidence of the dermatosis in a group of soldiers during the war ranged from 4 to 26 per cent.[32] The actual incidence is probably somewhat less than indicated by these observations, but it must be remembered that a greater frequency is to be expected among such a selected group as persons ill with other diseases.

29. Ruch, D. M.; Brunsting, L. A., and Osterberg, A. E.: Use of Vitamin A Tolerance Test in Certain Cases of Dermatologic Disorders, Proc. Staff. Meet., Mayo Clin. **21**: 209, 1946.

30. Youmans, J. B.; Patton, E. W.; Sutton, W. R.; Kern, R., and Steinkamp, R.: Surveys of the Nutrition of Populations: (3) The Vitamin A Nutrition of a Rural Population in Middle Tennessee, Am. J. Pub. Health **34**: 368, 1944.

31. Bessey, O. A., and Lowry, O. H.: Nutritional Assay of 1,200 New York State School Children, Report of the New York State Joint Legislative Committee on Nutrition, 1947.

32. Report on Project No. 30: Test of Acceptability and Adequacy of United States Army C, K, 10-in-1, and Canadian Army Mess Tin Rations, Armored Medical Research Laboratory, Fort Knox, Ky., Office of the Surgeon General of the Army, Washington, D. C., 1944.

Treatment.—Except for scarring of such tissues as the eyes, the lesions of vitamin A deficiency should respond to adequate treatment with the vitamin. In accordance with general principles, functional changes, represented by the night blindness, should respond promptly, and structural changes, such as the dermatosis, more slowly, the latter often only over a period of several weeks. Except in unusual circumstances, small to moderate doses—10,000 to 40,000 units daily—are all that are needed. There is no evidence that structural lesions will respond more rapidly to excessively large doses unless there is difficulty of absorption. Two exceptions to this general principle probably exist: in patients, especially infants or children, with acute keratomalacia and in infants with involvement of the bronchi, atelectasis and pneumonia. In such instances much larger doses, 50,000 to 100,000 units, may be used empirically with the hope of more quickly stopping the process before irreparable damage or death occurs. There may be a paradoxic exacerbation of symptoms at the onset of treatment (due to a sudden sloughing of large masses of cornified epithelium). Occasionally, massive doses, 500,000 units or more, may be required to overcome difficulties of absorption or individual peculiarities.

The preparations of choice are the fish liver oils or concentrates. There are many forms, containing up to 60,000 international units per hundred milliliters. Care should be taken, when massive doses are used, to guard against overdosage with vitamin D, which is present in relatively high concentration in some preparations. Large doses may cause nausea and anorexia. Recently, parenteral preparations have become available, but they are rarely needed. Aside from the specific treatment, little is needed but ordinary cleanliness.

VITAMIN D

Rickets is the result of a deficiency of vitamin D, and it is interesting to note that all stages of the deficiency, from mild to severe, are thought of and written of as rickets and not, as has been the case with some other vitamins, called rickets only when clearly manifest and given some other name when less severe. Rickets is a disease of growing bone and hence does not occur in adults. Vitamin D deficiency in adults is perhaps best called osteomalacia.

Confusion has sometimes arisen because other factors may affect the occurrence of rickets, particularly experimentally and in animals. For example, grossly abnormal diets favor the development of rickets (actually cause it in some animals); other deficiencies, notably that of calcium, may complicate rickets, with a resulting tetany, and a clinical picture resembling rickets but unrelated to a deficiency of vitamin D can occur. Rickets may also occur in premature infants as a result of calcium and phosphorus deficiency when human milk is fed and not supplemented. A deficiency of vitamin D is, however, the common and primary cause of rickets.

The nature of the group of substances included under the name vitamin D, together with relationships and action, has been described elsewhere.[33] Whether other effects are attributable to a deficiency of these substances and whether they are concerned with some of the nonosseous manifestations of rickets is unknown.

The clinical manifestations of rickets are too well known to warrant extensive description here. They

33. Handbook on Nutrition, chap. 10: To be published.

involve the skeleton primarily [34] and, as in all deficiency disease, range in severity from slight, undetectable changes to those severe enough to be fatal. The changes are primarily structural, although disturbances in function directly dependent on structural abnormalities do occur. It is important to remember that deformities, which are the "scars" and residue of structural changes, may persist after the deficiency of vitamin D has been relieved and the rickets cured, leaving forever mute evidence of the illness. Such deformities or scars should never be interpreted as indicating an existing deficiency of vitamin D.

The earliest detectable change in rickets probably is the increase in alkaline phosphatase. This is soon followed by a decrease in the blood phosphorus. The second stage is the roentgenographic appearance of abnormalities in the skeleton, detectable only roentgenographically. The third is the development of physical changes observable on ordinary examination. These range from slight to gross alterations in skeletal structure, with various accompanying signs and symptoms. Other symptoms, not related to the skeletal system, may be present.

Because rachitis occurs in growing bone, the most active lesions are to be found in the part of the bones growing most rapidly, the junction of the epiphysis and diaphysis, and corresponding areas in the flat bones. The earliest changes in the bones are microscopic and consist of a disorderliness and disarrangement of the normal pattern, which is one of great orderliness and regularity. In the zone of proliferation, the cartilage cells, instead of degenerating evenly and uniformly just before the capillaries reach them, fail to degenerate and be absorbed. The region of the proliferating cartilage enlarges because the cells fail to die, and large masses pile up in irregular fashion. The capillaries eventually reach and destroy them, but the process is irregular. The line of advance, instead of being even, is irregular. Even where the capillaries do advance, masses or islands of cartilage cells may persist. Cells on the outside of the mass are abnormal in appearance and staining. Some of the original matrix is destroyed, but some remains, calcified and uncalcified. On this, osteoblasts lay down osteoid tissue and build irregular chondro-osteoid trabeculae. Depending on the stage of the rickets, this osteoid bone either completely fails to calcify or does so irregularly and incompletely.

Into this rachitic intermediate zone extrusions and enlargements of the cartilage canals penetrate from the distal side in the more severe cases and sometimes from the shaft and side (perichondrial) as well. The amount of connective tissue brought in by blood vessels may be greatly increased.

It is this rachitic intermediate zone which is responsible in large measure for the deformities. It causes enlargement of the ends of the long bones as they increase in length and pushes the centers of ossification of the epiphysis further from the shaft. Being osteoid (soft) bone, it is easily bent by the forces of posture, weight-bearing and muscle pull. The direction of the line of new growth is thus changed, and growth continues to follow the new direction even when it is at a considerable angle to the line of the shaft previously formed Greater in size, the intermediate zone becomes too large for the shaft, spreads it and deflects the trabeculae outward. Increased thickness of the shaft develops from increased perichondrial deposit of osteoid tissue. Improper calcification and increased decalcification of the shaft softens the latter, which bends in various directions. Bending of the shaft is usually one of the later deformities.

Changes similar to those described at the epiphysial-diaphysial junction of growing long bones occur in all bone in the process of formation, the osteoid bone being deficient in calcium salts. Such changes can be seen in the cancellous portions of long bones, in the cortex along the lacunas, in the tables of the skull and elsewhere in the skeleton.

Repair begins when vitamin D deficiency ceases, and it begins in the area where normal ossification would be occurring had not rickets intervened, leaving the abnormal area behind to be straightened out later. The area where normal ossification begins appears as a dense, white, transverse line of healing on roentgenograms. Next, focal areas of healing appear and spread; gradually the capillaries and columns of cartilage cells assume their regular form, and the normal process of decalcification, ossification and recalcification takes over. Because there has been an abnormal, excessive overgrowth of osteoid tissue, there is a gradual selective absorption, which reduces the size of the mass, straightens it out, rearranges it and reduces the deformity. The degree of restoration may be surprisingly great and may occur over months or years.

Defects in tooth structure can be assumed to occur in rickets, although they may not be apparent and when present may be difficult to distinguish from the injury caused by lack of vitamins A or C. Defects are most frequent in permanent teeth, because rickets usually occurs at the time they are calcifying, but defects can occur in the temporary teeth.

Other pathologic changes consist of slight hypertrophy of the parathyroids and perhaps some atrophy of the thyroid cells. The fibrosis and atrophy of muscles sometimes observed is probably not specific for rickets.

The changes in nongrowing bone, which may be the result of vitamin D deficiency, are described in the section on calcium deficiency and osteomalacia. Albright and his associates have reviewed and summarized their studies of this condition and have presented a critical review of the literature.[35] According to them, vitamin D deficiency and the osteomalacia accompanying it is of three kinds: (1) that due to simple lack of vitamin D; (2) that due to vitamin D resistance, and (3) that due to vitamin D deficiency accompanying steatorrhea. There is little doubt that, as these authors indicate, simple lack of vitamin D in adults is uncommon in this country. That due to steatorrhea is, of course, a conditioned deficiency occurring under a variety of conditions causing the steatorrhea. The vitamin D resistant group is similar to the group with "resistant rickets" already mentioned. However, in one case recently reported by McCance,[36] the resistance (and deficiency) apparently did not develop until the patient was 15 years old. McCance states that other similar cases have been reported. The patient reported by McCance showed pseudofractures

34. Follis, R. H., Jr.: The Pathology of Nutritional Disease—Physiological and Morphological Changes Which Result from Deficiencies of the Essential Elements, Amino Acids, Vitamins and Fatty Acids, Springfield, Ill., Charles C Thomas, Publisher, p. 291, 1948.

35. Albright, F.; Burnett, C. H.; Parson, W.; Reifenstein, E. C., Jr., and Roos, A.: Osteomalacia and Late Rickets: The Various Etiologies Met in the United States with Emphasis on That Resulting from a Specific Form of Renal Acidosis, the Therapeutic Indications for Each Etiological Sub-Group, and the Relationship Between Osteomalacia and Milkman's Syndrome, Medicine **25**: 399, 1946.

36. McCance, R. A.: Osteomalacia with Looser's Nodes (Milkman's Syndrome) Due to a Raised Resistance to Vitamin D Acquired About the Age of 15 Years, Quart. J. Med. **16**: 33, 1947.

on roentgen examination similar to those described by Milkman [37] and known as Milkman's syndrome. Albright and his co-workers consider this syndrome a simple manifestation of osteomalacia and not a specific disease entity.

In general, the symptoms of rickets are mild and rather vague. Analysis of the food intake is of little value, except in relation to the use of supplements, milk fortified with vitamin D, cod liver oil and similar substances. The need for these substances is so great ordinarily that lack of them warrants a tentative diagnosis. The physical signs of the disease are the deformities and abnormalities of the skeleton. Usually the latter are the first things noted. Craniotabes, which occurs at about 3 months of age, is usually the first to be found, affecting a few small areas on the back of the head. The cranial sutures are widened and the edges soft. Later, the "rachitic rosary," enlargement of the costochondral junctions and the wrists, distal ulna and radius are observed. Craniotabes may not occur if the disease begins later. Constitutional symptoms are lacking in mild or moderately severe cases, and the infant may appear well, though rather pudgy and pasty. With severer rickets there are restlessness, head sweating, irritability and weakness, though it has been questioned whether some of these are truly a part of rickets. Generally, the severer the deficiency, the earlier symptoms and signs appear.

During the middle part of the first year, unless deficiency is relieved, the craniotabes is more widespread and weakness is greater. Cranial deformities from pressure appear on the back and side of the head. When the patient is 8 or 9 months of age the craniotabes disappears, but the cranial deformities increase, and frontal and parietal bosses cause the "square head" and "olympian brow." The fontanelles remain open, the frontal widely. Additional deformities of the chest appear: Harrison's groove, depression of the sternum, "chicken breast" and lateral trough. The enlargement of the ends of the ulna and radius, as well as of the other long bones, increases but may be masked by fat. The child is less active and may have a "pot belly."

It is evident that the progress of the disease and the development of deformities depend greatly on the supply of vitamin D, intentional or fortuitous. Thus the disease may progress rapidly and in severe degree, may be held at relatively static levels of moderate severity, may be nearly completely relieved with almost no evidence of activity or may shift between these various states. If the rickets continues in a moderate or severe form during the first and second years, the signs persist or increase, except for the craniotabes. If the onset occurs then, the changes are apt to be pronounced, because of the effect of such forces as those induced by various postures. Often the child is too weak to stand and to walk. In such cases, the deformities of the head are greater, chest deformities increase, the spine becomes bowed (kyphosis) and the more severe deformities of the extremities, such as bow legs, appear. Dentition is delayed, and defective teeth are evident. Roentgenograms may show one or more greenstick fractures of the long bones. The anterior fontanelle may remain open at 2 years of age or older. Weak children, raised to a sitting posture, assume a characteristic posture with the legs crossed and the hands supporting them at their sides. Standing and walking increase the deformities of the legs and pelvis.

Deformities are a product of the severity of the deficiency, the developmental stage of the parts affected, the rate of growth and the physical stress to which the parts are subjected. Reciprocally, the more rapid the growth, the more severe the rickets (because of the increase in the requirements of vitamin D).

Craniotabes, which is not specific for rickets, is essentially due to lack of calcification and consists of a softening and thinning of an area of the skull, which indents and rebounds, often with a crackle. Similar changes occur in osteogenesis imperfecta, in hydrocephalus and even in some normal (especially premature) infants. The areas are spotty and nearly always posterior in rickets, with ill defined edges varying in size from small (2 cm.) to extremely large. They are not usually bilateral. They usually occur at 3 or 4 months of age. In osteogenesis imperfecta the areas are larger and more widely distributed. Those in normal infants usually are unilateral, occur along suture lines and disappear before rickets appears. Craniotabes is called the "most reliable, single, bedside sign of rickets."

Bosses on the skull occur on the surface because the bone there is mainly of periosteal origin. Although the head is enlarged, the cranial cavity is not increased.

The commonest chest deformity, the "rachitic rosary," may be difficult to detect in mild cases because the enlargement may be mainly on the inner surface. If the rickets is at all severe, healing may leave permanent deformities. In most cases respiratory obstruction is needed, besides rickets, to produce a pigeon breast. Kyphosis develops with the sitting posture, lordosis with standing and walking. Lack of muscle tone is a factor. The worst deformities of the pelvis occur when the rickets is prolonged into childhood, especially if the child can stand and walk despite the rickets. These deformities are most familiar and important to the obstetrician as deformities in the childbearing woman.

Deformities of the extremities usually occur rather late and are associated with sitting, standing and walking. A variety of deformities may be present; there is both lateral and anterior bowing (saber shin, bowleg and knock knee). As growth occurs, the deformities shift their position, the forward bend of saber shin ascending from its location just above the ankle in infancy to the junction of the lower and middle third of the tibia. In contrast to the saber shin of congenital syphilis in which the thickening is anterior, the rachitic thickening is irregular and more posterior than anterior. Coxa vara, or a more acute angle of the neck of the femur on the shaft, can cause a waddling gait.

Nystagmus and head rolling and shaking may appear in addition to head sweating, irritability and restlessness. The nystagmus may occur in any plane and in either or both eyes and, if bilateral, is convergent. Its exact relation to the rickets is unknown.

Diagnosis.—The most practical early diagnosis probably is made by roentgenogram. However, this is neither easy nor certain in the earliest stages, and differences of opinion in respect to the interpretation of the roentgen findings may be encountered in any particular case. Nevertheless, long before any physical signs become clearly manifest, the roentgen changes are definite, and the changes in the alkaline phosphatase and phosphorus levels in the serum are available for supportive evidence for a diagnosis which should be suggested to the alert physician by the history of the infant. Difficulty and error may occur in routine examination of apparently well infants if the disease is in its early stages. In the more advanced stages of

37. Milkman, L. A.: Multiple Spontaneous Idiopathic Symmetrical Fractures, Am. J. Roentgenol. 32: 622, 1934.

the deficiency, the usual symptoms and physical changes should be adequate for the establishment of the diagnosis. Such patients should reach the physician only when they have not previously had medical care.

With the roentgenograms, one can examine the lesions at short intervals, observing the effect of treatment. Because of accessibility and convenience, as well as early occurrence of changes, the lower radius and ulna are the usual sites for the clinical roentgen examination. The principal changes are cupping, spreading, spur formation, fringing, stippling and changes in the shaft. None are specific, and all are subject to interpretation. Cupping is a concavity at the end of the shaft and is not consistent. Spreading, referred to in the discussion of the pathology, is a widening of the end of the shaft and may or may not be accompanied by cupping. It occurs in scurvy also. Spurs are calcified lines extending from the cortex of the shaft down along the side of the proliferating cartilage. The alinement is often poor. Spurs occur in congenital syphilis and to a slight extent in normal bones at times. Fraying and fringing refer to narrow, irregular, tangled lines running from the shaft into the cartilage. In the early stages they are thin and short, in more severe cases thicker and longer. They are reliable but not particularly early signs. They occur in syphilis also. Stippling gives an irregular, dotted appearance to the end of the shaft. It may appear early, but is also present late in the disease.

Eliot and Park's[38] "early," in contrast to "very early," signs consist of a lack of sharp definition of the edge of the distal end of the ulna away from the radius and a decreased density of the cortex in the same area. This should not be confused with the normal irregularities associated with muscle attachment there. Similar changes are found in the middle of the shaft of the radius and the proximal end of the ulna on the radial side as early evidence of periosteal proliferation and decreased cortical density. "Atrophic" changes are late but characteristic. They consist of decreased density, with irregular trabecular markings, thin cortex and hair-like shadows extending out from the shaft. The cortex may be thickened on one side and the marrow cavity narrowed. There may also be such severe changes as fractures, distortions and displacements.

The roentgenogram discloses changes induced by treatment (healing), which is also of diagnostic value because it checks the therapeutic trial. Recovery is marked by the deposit of lime salts and is seen at the junction of cartilage and shaft as a thin, transparent line, faint and incomplete at first and later broad and heavy, even double. It appears in the region where calcification would be occurring had not rickets developed and hence is in the distal portion of the intermediate zone at a considerable distance from the end of the shaft, the distance depending on the duration and severity of the disease. As the osteoid trabeculae become calcified, the intermediate zone shows spotty shadows, and calcification appears in the periosteal encasements. Alternate periods of remission and relapse due to treatment or natural variations cause various combinations of activity and healing.

Measurement of the concentration of alkaline phosphatase in the blood, which rises in rickets, is useful in diagnosis and may give evidence before changes in the roentgenogram can be detected, thus being helpful in the diagnosis of early rickets. Also, the concentration remains elevated long after treatment and healing are begun, returning to normal only after the latter is complete or nearly complete. Thus, it is a better measure of adequate treatment than the roentgenogram and has prognostic value. The concentration is usually expressed in Bodansky units in this country. Normal values for infants are 3 to 12 units. No generally accepted standards are available for older children or adults, in whom the significance of variations is not well established. A survey of a large general population gave values for adults[39] from 1.5 to 5.0 Bodansky units, with a mean of approximately 3.0 units. Variations in serum phosphatase values may occur in conditions other than rickets or vitamin D deficiency, but this is of little practical importance in relation to its use in the diagnosis of rickets in infants. It is a greater problem in older children and adults.

The determination of inorganic phosphorus in the serum is a useful clinical test for rickets but has certain drawbacks. In early or slight rickets the values fall in the doubtful range. Treatment causes a prompt rise to normal, despite persisting disease and incomplete recovery, and hence the determination does not accurately reflect the actual progress or adequacy of treatment. It is of little value in vitamin D deficiency in adults, and in the intermediate period of childhood and adolescence it is difficult to tell in a given case whether the values are abnormal. The generally accepted normal value for infants is 5 to 7 mg. per hundred milliliters, with few well infants below 5 mg. and with 4 mg. the beginning level for rickets, in which values may be even lower than 2 mg. In adults the normal range is from 3 to 4.5 mg., and children and adolescents have values between those of infants and adults. Determination of the concentration is of little or no value in adults.

The concentration of calcium in the blood is often determined in suspected rickets and vitamin D deficiency. In rachitic children and infants, the values are usually normal (9 to 11 mg. per hundred milliliters), though they may be reduced. When these values are low, the rickets may be complicated by tetany, but this is unusual. The normal values are the same in adults, and a lowered concentration of calcium in the blood caused by vitamin D deficiency, even with a low intake, is uncommon.

The therapeutic test is of great value in rickets, particularly when the effects of treatment are checked with repeated roentgen and blood examinations. In adults with osteomalacia the relief of symptoms, pain in particular, is helpful.

Incidence.—The actual incidence of rickets is difficult to determine. The general belief is that with modern knowledge of means of prevention on the part of physicians and the public and with the availability and widespread use of effective preparations of vitamin D, the disease is now infrequent in this country. There is evidence, however, that this belief is overly optimistic, particularly in older children. Follis, Jackson and Park,[40] on the basis of microscopic examination of autopsy material, have reported an incidence of as

38. Eliot, M. M., and Park, E. A.: Brennemann's Practice of Pediatrics, by Various Authors, edited by Irvine McQuarrie, Hagerstown, Md., W. F. Prior Company, Inc., 1948, vol. 1, chap. 36.

39. Youmans, J. B.; Patton, E. W.; Sutton, W. R.; Kern, R., and Steinkamp, R.: Survey of the Nutrition of Populations: (4) The Vitamin D and Calcium Nutrition of a Rural Population in Middle Tennessee, Am. J. Pub. Health **34**: 1049, 1944.

40. Follis, R. H., Jr.; Jackson, D., and Park, E. A.: The Problem of the Association of Rickets and Scurvy, Am. J. Dis. Child. **60**: 745, (Sept.) 1940. Follis, R. H., Jr.; Jackson, D.; Eliot, M. M., and Park, E. A.: Prevalence of Rickets in Children Between 2 and 14 Years of Age, ibid. **66**: 1, 1943.

high as 48 per cent in infants aged 3 to 19 months and 46 per cent in children up to 12 years of age. In infants the use of the roentgenogram and other of the finer means of diagnosis indicates that minimal forms are more frequent than is commonly thought.

It should be realized that the incidence is greatly affected by the environment. Variations in ultraviolet radiation, dependent on season, latitude, smoke and housing, affect the requirements of dietary vitamin D. The incidence of rickets is greater in crowded, smoky cities, among infants born so that their most susceptible period (4 to 6 months) comes during winter and in dark-skinned races. Also, the more the confinement indoors, the greater the incidence.

It must be remembered, however, that in pointing out the probably rather large frequency of rickets, I am referring mainly to mild or minimal forms of the disease. The incidence of florid, severe rickets has undoubtedly been greatly reduced. It must also be remembered that some, at least, of present day rickets is the result of greatly improved general health and care of infants, leading to more rapid growth and, hence, to greater requirements of vitamin D than have been generally appreciated. Some idea of the incidence of rickets in a rural area is furnished by the results of a survey [39] of some 94 subjects under 3 years of age which indicated an incidence of around 24 per cent. Even this observation is made less significant, however, by one's inability, in certain cases, to distinguish between active and inactive rickets and the lack of close correspondence between the several criteria used in diagnosis. It does, however, suggest the total rickets "experience" in the group.

Congenital rickets is rare, but it does occur and is apt to be severe in premature infants and twins.

Treatment.—Rickets should be prevented rather than treated, but there are always some children who escape preventive measures in one manner or another and require treatment. Standard preventive measures for the usual infant involve the administration of 200 international units of vitamin D from birth. This dose should be increased in a few days to 400 units. All infants should be protected during the first two years of life, and, in the light of present knowledge, it would be well if some degree of protection were used during the growing period. Protection for an entire season can be afforded by the administration of a single large dose of vitamin D. This procedure has certain advantages, among them being the greater assurance that the vitamin is actually taken and the protection really given. For these purposes a dose of 75 mg. of calciferol (vitamin D_2) with an activity of 300,000 international units given in 1 cc. of peanut oil after a milk feeding has been recommended.[41] However, there is a possibility of at least mild toxicity with such a procedure.

Ordinarily, after the growth period the requirements will be met adequately by the usual exposure to sunlight and the preformed vitamin D consumed in the food. Milk fortified with vitamin D contributes to these sources but should not be depended on for protection during the more susceptible period of infancy unless intake provides at least 400 units per day. For supplements, concentrated preparations of vitamin D—cod liver oil, fortified fish liver oil (halibut), concentrated fish liver oils (percomorph) or viosterol in oil—are needed. The fish liver oils contain vitamin A, which I believe is a decided advantage. Fish liver oils contain vitamin D of animal nature. Viosterol in oil has the advantage and disadvantage of small volume. The concentration is adjusted to provide 222 units per drop, which permits the giving of large doses in a form not unpleasant to take and easy to administer. The small amount can easily be "lost," however, in containers. Vitamin D in propylene glycol or alcohol provides a preparation miscible with water and hence easily incorporated in the infant's formula. All preparations should be prescribed and administered in adequate dosage based on the concentration of the product in terms of international units. Physicians should know the strength of the preparations they employ and should prescribe on a unit basis.

Protection should be afforded to pregnant women, especially during the latter half of pregnancy, and to nursing mothers. Both mother and child will be benefited. Moderate doses of 400 to 800 units a day will be sufficient except in unusual cases.[42] Similar amounts will suffice for invalids and others kept indoors. Special attention to the intake of calcium and phosphorus must be given to twins and premature infants.

Much more active treatment is required for the cure of rickets. Daily doses of 1,200 units will be sufficient in ordinary cases. Much larger doses, 5,000 to 10,000 units per day, will sometimes be required. When extremely large doses are used, the concentrated preparations are a practical necessity. About three weeks are required to determine the effectiveness of a given dose, and one should not hesitate to increase the dose drastically if improvement does not occur or is unsatisfactory. The concentration of inorganic phosphorus in the serum should begin to increase in about ten days, and roentgenographic evidence of healing should appear in about three weeks, but the mere presence of these changes does not mean that the cure is complete. The phosphatase concentration will remain elevated until a cure is obtained. Deformities are corrected slowly, and old deformities (scars) should not be interpreted as evidence of active rickets.

As the disease is controlled, the dose can be reduced, but amounts larger than the usual protective doses should be continued for several months. The aim in the treatment of rickets is to stop the progress of the disease as soon as possible and bring about a cure before deformities can develop or increase. For this reason, large doses may even be lifesaving in occasional cases of severe rickets in which the weakness of the ribs may cause danger of asphyxiation.

Occasionally, cases of so-called refractory rickets are seen. These are usually found in children 3 years of age and over, who seem to have some individual peculiarity with respect to vitamin D. Most of these will respond to extremely large doses, 50,000 to 100,000 units. In rare cases 1,000,000 to 1,500,000 units may be needed to secure an effect.[35] High maintenance doses are also necessary. Refractoriness suggests an incorrect diagnosis and, especially, the presence of one of the rickets-like diseases caused by metabolic disturbances.

In rickets complicated by tetany, sufficient calcium may be supplied with the milk, provided the intake is adequate. Treatment of rickets with vitamin D may precipitate tetany by the sudden withdrawal of calcium from the blood to deposit in the skeleton under the early and partial healing effect of the vitamin. This effect is more likely to occur in the severer cases of

41. Krestin, D.: Treatment of Rickets with Single Massive Doses of Vitamin D_2, Lancet **1**: 781, 1945.

42. Dieckmann, W. J.: Diet from the Viewpoint of the Obstetrician, Nutrition Rev. **6**: 129, 1948.

rickets and, if anticipated, can be prevented by the administration of calcium. Calcium will also relieve tetany. Calcium can be given as the chloride, lactate or gluconate, but the chloride is somewhat more effective in these circumstances. An initial dose of 3 to 4 Gm. followed by 1 Gm. three or four times daily, with the dose gradually decreasing after three or four days, is usually adequate.

In adults, vitamin D deficiency is usually mild and easily relieved by ordinary doses of vitamin D. It is usually helpful if some calcium is given in addition to the vitamin, since many cases in adults represent a dual deficiency. Doses of 1,200 to 1,600 units per day will ordinarily suffice. Failure of the vitamin to relieve the condition (a common experience) indicates that the simple efficiency of vitamin D, with or without calcium deficiency, is not the cause and that some other disease, such as hyperparathyroidism, is present.

Hypervitaminosis D.—Poisoning from vitamin D in the prevention and cure of rickets is uncommon, although doses of 1,500 units continued over a period of months may be mildly toxic. Patients with so-called resistant rickets tolerate the larger doses needed without harm. However, vitamin D is sometimes used in tremendously large doses in the treatment of a variety of diseases. For these purposes doses as large as 1,000,000 units or more daily have been advised. In these circumstances poisoning can occur. Early symptoms are anorexia, nausea, headaches, diarrhea and, in children, pallor and lassitude. There is an increase in the calcium content of the blood, although there need be no direct relation of symptoms to the blood calcium. Calcium crystals and casts may be found in the urine, and metastatic calcification may occur.

VITAMIN K

Vitamin K is rather abundant in food and is formed in the intestine by the action of bacteria; therefore, deficiencies of the vitamin are rarely the result of a dietary inadequacy. Rather, a deficiency occurs because of some condition which interferes with the production of the vitamin in the intestine or its absorption from the gastrointestinal tract. In the latter category are included various gastrointestinal disorders such as ulcerative enteritis. Also, because it is a fat-soluble vitamin, the various conditions interfering with the absorption of fat, such as obstructive jaundice, sprue and celiac disease may interfere with the production of vitamin K. As far as is known, its sole function in man is its participation in the formation of prothrombin. Prothrombin is one of the substances involved in the clotting of blood. When there is a deficiency of prothrombin, there is delay in or failure of clotting, with the result that hemorrhage may occur. A deficiency of vitamin K, by lessening prothrombin formation, delays clotting and is manifested by hemorrhage. It is believed that prothrombin is formed in the liver, but the exact part which vitamin K plays in its production is unknown. It is to be remembered, however, that other factors, such as the function of the liver itself, are concerned, and, in some cases of liver damage, prothrombin formation may be deficient although even excess quantities of vitamin K are available.

The abnormality resulting from vitamin K deficiency itself can be considered entirely functional and the organic changes simply those of the resulting hemorrhage. These changes do not differ from those of hemorrhage of other origin. It should be remembered, however, that the hemorrhage in vitamin K deficiency is not spontaneous; it follows trauma, even though that trauma may be relatively slight. The defect is in the clotting after bleeding has begun. Vitamin K deficiency does not precipitate bleeding.

The clinical picture of the deficiency, therefore, is that of hemorrhage, divided into three main groups: (1) hemorrhage of the newborn; (2) hemorrhage associated with disorders of intestinal absorption, particularly those resulting from obstructive jaundice or interference with the production of vitamin K by the bacteria in the intestine, as might be the case after prolonged use of such drugs as the sulfonamides, and (3) a simple form of hemorrhage accompanying general malnutrition and inadequate intake of food. The last is, as previously stated, uncommon, the bleeding being present in the simple form of subcutaneous hemorrhages, petechiae and purpura.

In the newborn, the disease is striking and clear cut. As might be expected, it is practically self-limited, since vitamin K production in the intestine brings it to a close if death does not occur earlier. This results from the fact that the principal source of vitamin K in infants is its production by bacteria in the intestine[43] and that the intestine of the newborn child is sterile and some days are required for the development of an intestinal flora, since only a small amount may be given the infant by its mother. The disease is also rather clearly defined in point of onset and duration, rarely beginning before the second or third day of life, with recovery by the seventh or eighth. Death rarely occurs after the third day. There is usually bleeding at multiple sites, such as skin, external mucosal surfaces, hollow viscera, brain and lungs, with the mucous membranes being especially affected. Death results from debility and loss of blood. Accompanying the hemorrhage, which is usually oozing in nature but persistent, there may be fever and diarrhea.

The relation of this deficiency and the hemorrhagic state to birth trauma, cerebral birth injuries, and resulting spastic paraplegia and related disorders is not clear. It has been suggested that, although some hemorrhage might well result from birth trauma, it usually would not, except in cases in which there might be a diminished prothrombin level, be sufficient to cause significant injury. However, vitamin K deficiency and diminished amounts of prothrombin might exaggerate and prolong the initial hemorrhage into excessive bleeding. Certainly, other hemorrhages occur in these circumstances and are clearly visible, but they lack the potential seriousness of the cerebral (meningeal) bleeding.

Clinically, the greatest amount of vitamin K deficiency is probably that associated with and resulting from jaundiced states, the deficiency resulting from the interference with the absorption of fat and, hence, of vitamin K from the intestine. A second considerable number of cases are those in which the deficiency accompanies various diseases of the intestines with disorders of absorption, including sprue. In persons with diseases amenable to surgical intervention, the bleeding is most important in relation to operative procedures, to which it constituted a threatening and dangerous complication in the days before vitamin K. In other cases it is familiar as the symptomatic purpura of malnutrition, although even more extensive bleeding can occur in these circumstances.

43. Kornberg, A.; Daft, F. S., and Schrell, W. H.: Mechanism of Production of Vitamin K Deficiency in Rats by Sulfonamides, J. Biol. Chem. **155**: 193, 1944.

Diagnosis.—Vitamin K deficiency is detected by the appearance of hemorrhage and by a determination of the concentration of prothrombin in the blood. For practical purposes, the deficiency is confirmed by the increase in prothrombin following treatment with vitamin K. The deficiency should be suspected from a knowledge of the patient, and confirmed by the prothrombin test, and the hemorrhage should be prevented if possible. Fairly simple and reliable tests for the concentration of prothrombin exist and can be repeated readily. Of these, those of Quick and Grossman [44] and Ziffern, Owen, Hoffman and Smith [45] are the most useful and satisfactory clinically. Vitamin K deficiency is one of the few deficiencies in which a quantitative measurement of the body's vitamin store or reserve is possible, permitting an accurate determination of the point at which a true deficiency occurs. At a prothrombin level below 20 per cent of normal, a delay in clotting appears. The test should be made in all cases of suspected deficiency. The tests are not specific, however, and should always be checked by the administration of a few doses of a suitable vitamin K preparation.

Incidence.—The incidence of vitamin K deficiency in the general population is unknown. Most studies have included only special groups, such as the newborn and pregnant women. The deficiency is known to occur frequently in patients with sprue, jaundice and other diseases which interfere with intestinal absorption, especially fat absorption. It is also found in malnutrition. It is apparent, therefore, that, except for the newborn, the disease will most often be found among patients ill with other disease.

The incidence among the newborn is uncertain, and differences of opinion concerning it exist among obstetricians. Eastman [46] believes that among his patients, at least, hemorrhagic disease of the newborn is relatively common and that the dramatic decrease in mortality rates in recent years of both mature and premature infants is partly attributable to the routine use of vitamin K.

Treatment.—A number of "artificial" vitamin K's, more potent than the natural form, have been developed. One of these, 2-methyl-1, 4-naphthoquinone, is the preparation commonly used in treatment, under the name menadione U. S. P. A water soluble form, menadione sodium bisulfite U. S. P., does not require the concomitant use of bile salts when given by mouth to jaundiced patients. The water-soluble form contains not less than 49 per cent menadione. Preparations of both forms of menadione are available for injection.

Vitamin K is somewhat more effective and faster in action when given by mouth than by parenteral injection, but there are some advantages to the latter route in some cases. Vitamin K is often given prophylactically, particularly to patients with diseases which may lead to vitamin K deficiency and to the newborn. For the latter purpose, the prophylaxis is usually accomplished by treating the mother for a short period before delivery. For this purpose, the equivalent of 1 mg. of synthetic vitamin K (menadione) is given daily for several days just prior to delivery or once weekly during the last few weeks of pregnancy and at the onset of labor. The advisability of routine treatment of the mother to prevent hemorrhagic disease of the newborn is still debated. According to Eastman,[46] vitamin K should be given to all women as soon as labor starts.

If the infant is treated directly, the equivalent of 0.5 mg. is given at birth and 1.0 mg. daily is given in divided doses for two or three days thereafter. It may be placed on the back of the infant's tongue or added to the feeding or water. Protection is particularly necessary for infants under a week of age who are to undergo surgical procedures.

Other patients can be protected in the same way and with approximately the same doses. The effect of treatment can be checked and a guide to dosage obtained by a repetition of the prothrombin concentration tests. If the vitamin cannot be taken by mouth, it can be given by duodenal tube or by parenteral injection. Doses larger than 5 mg. are rarely needed.

If a deficiency already exists, prompt treatment is important, especially in the newborn. Prophylactic doses will usually suffice for treatment of newborn infants. These prophylactic doses should be increased if the response does not appear or is delayed. Progress should be checked with the prothrombin test. Postoperatively, caution must be taken that loss of blood and subsequent dilution with fluids does not reduce previously adequate vitamin K levels to pathologic levels. In some patients treatment must be continued at intervals.

In treatment of prothrombin deficiency resulting from the administration of dicumarol,* 64 mg. of menadione sodium bisulfite administered intravenously has been found effective in some cases, though the response is sometimes undesirably slow. This dose is equivalent to 40 mg. of menadione. Occasionally this condition does not respond to these large doses of vitamin K; when it does not, whole blood should be administered.

VITAMIN E

It is still customary to include vitamin E among those vitamins for which a relationship to deficiency and disease in man has been demonstrated. The correctness of this may be doubted seriously, and there seems little justification at present for the inclusion of a description of the supposed symptomatology and pathology of vitamin E deficiency in a discussion of the vitamin deficiency diseases of man. There is nothing in the well known signs, symptoms and pathologic changes of repeated and threatened abortion to indicate that they bear any specific relation to a deficiency of the tocopherols, except in some extremely dubious responses, dubious in the clinical as well as statistical sense, to treatment with the vitamin. None of the other pathologic changes noted in animals—testicular degeneration, degenerative changes in the muscles, pigmentation of the uterus and the muscular layers of the seminal vesicles, degeneration of the convoluted tubules of the kidney and changes in hair, skin and various endocrine glands—have been shown to have their counterpart in man. Neither have reports of specific effects of the vitamin in such diseases as muscular dystrophy in man been corroborated. All this is the more important because vitamin E and a number of closely related substances are well-known, identified, isolated and synthesized substances, a situation which usually is helpful in establishing function and relationship to disease. This does not mean, however, that a relationship of vitamin E to requirements and disease in man will not be established, simply that so far it has not been done.

44. Quick, A. J., and Grossman, A. M.: Nature of Hemorrhagic Disease of Newborn; Delayed Restoration of Prothrombin Level, Am. J. M. Sc. **199**: 1, 1940.

45. Ziffern, S. E.; Owen, C. A.; Hoffman, G. R., and Smith, H. P.: Control of Vitamin K Therapy: Compensatory Mechanisms at Low Prothrombin Levels, Proc. Soc. Exper. Biol. & Med. **40**: 595, 1939. McGrath, T. B.: Technique of the Prothrombin Time Determination, Am. J. Clin. Path. (suppl.) **3**: 187, 1939.

46. Eastman, N. J.: Prematurity from the Viewpoint of the Obstetrician, Am. Pract. **1**: 343, 1947.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION
535 N. DEARBORN ST. - - - CHICAGO 10, ILL.

Edited by
AUSTIN SMITH, M.D.

Associate Editor
JOHNSON F. HAMMOND, M.D.

Editor for Current Medical Literature, GEORGE HALPERIN, M.D.

Subscription price - - Twelve dollars per annum in advance
Cable Address - - - - "Medic, Chicago"

SATURDAY, SEPTEMBER 2, 1950

THE NATIONAL CONFERENCE ON AGING

Over 800 persons representing diverse professional fields and public groups met in Washington on August 13-15 to consider problems associated with the increasing proportion of older persons in our population. The conference was called, organized and conducted by staff members of the Federal Security Agency, with Mr. Clark Tibbitts as director. However, the detailed planning of program and scope of the conference was done by committees consisting chiefly of persons not employed by the federal government. It was a "working conference," in which 28 committees, grouped into nine sections, devoted four half-day sessions to discussion and preparation of written reports on such subjects as research, population changes, employment, income maintenance, health maintenance, rehabilitation, education, family life, housing, recreation, religious services, community organization and the recruitment and training of professional personnel with reference to the needs of older persons.

The Section on Health Maintenance and Rehabilitation was subdivided into seven subcommittees, which considered the topics of health promotion; etiology and epidemiology of diseases associated with aging; detection, treatment and care of diseases peculiar to higher age; care of disabled older persons; rehabilitation; environmental health needs, and community planning for the health of the aged. The following points were among those emphasized in the preliminary subcommittee reports of this section: (*a*) The characteristics of well adjusted older persons—the epidemiology of health—should be studied as well as that of disease. (*b*) There should be more accuracy in lay health education. (*c*) There should be more emphasis on geriatrics in medical education. (*d*) Caution should be used in promoting multiple screening programs, which are still in the experimental stage. (*e*) The development of more facilities for providing services at home which are now available only in hospitals or clinics. (*f*) Provision for senile patients with mild psychosis. (*g*) Formulation of basic standards for nursing homes. (*h*) Establishment of geriatric guidance centers for treatment, research, demonstration and training. (*i*) Development of community facilities for group activity and recreation of older persons. (*j*) Leadership of physicians and medical societies in developing integration of different community agencies to provide a balanced program to meet the health needs of older persons. The complete reports of the various subcommittees and sections will be published and made available to the public soon.

A national conference devoted to the exploration of all the problems of so large a segment of our population as the aged could scarcely be expected to produce new knowledge on the subject. Such a conference may have great value in focusing the attention of different disciplines and professions on the same set of problems, in accelerating understanding of diverse viewpoints, in formulating principles on which there is general agreement and in stimulating research and further planning. In order that the published report of the conference on aging may represent adequately and fairly the deliberations of the conference, opportunity should be given each subcommittee chairman to check the version of the report prepared by his subcommittee. Otherwise, conclusions reached by the democratic conference method may be slanted, perhaps inadvertently, in an undemocratic way.

COMICS IN THE FIGHT AGAINST GOVERNMENT-CONTROLLED MEDICINE

"The Sad Case of Waiting-Room Willie," a 16 page visual presentation in "comic book" form in color has just been published by the Committee on Public Medical Education of the Baltimore City Medical Society, to dramatize the unfavorable aspects of socialized medicine in a form that is readable, entertaining and nontechnical enough to reach all the voters. Briefly, the story of Willie is a collection of incidents, most of them from factual reports of occurrences under socialized medicine plans in other countries, but all happening to one poor waif, who is really sick and unable to get medical care under the New Utopia because the doctors he tries to consult are overrun with unsick patients who have also paid their health taxes and have an equal right "under the law" to take up the doctors' time. A copy of the book is available for inspection, and copies may be purchased in lots of one thousand or more, at cost, three cents each, from the Baltimore City Medical Society, 1211 Cathedral Street, Baltimore 1, Md., Attn.: G. R. Connolly, Publicity Director. To societies purchasing lots of a million or more, the rate is lower than for smaller orders.

In Maryland each physician has been asked to order at least 200 copies at three cents apiece. The city society cannot afford to distribute free more than a single copy to each physician. This booklet tells medicine's story in a form that will reach thousands who do

not read the more formal treatises prepared on the subject or listen to what promises to be a "purely educational" radio program. The Baltimore group is attempting to gain the widest possible distribution, aided by the Woman's Auxiliary of the society, the dentists, pharmacists and a number of civic organizations which have lined up with them. Leading magazine stands are accepting "test" consignments of 100 copies, which they can sell for five cents, paying the society the cost price of three cents. "Willie" should take his story all over the country as other societies approve him.

DERMAL LOSS OF IRON

In 1949 Mitchell and Hamilton[1] reported that as much as 6.5 mg. of iron are lost daily in the sweat. This previously unsuspected avenue of iron loss was subjected to detailed analysis by Adams and his associates[2] of the University of California at Los Angeles. With the method proposed by Leslie and Levin,[3] sweat samples were obtained from a full length rubber glove drawn over one hand and forearm. All subjects were in a fasting state. Two glasses of water were drunk before the test. The other arm was placed in a water bath at 110 F. during the one hour sweating period. An average of about 10 cc. of opalescent sweat was collected from each normal person. Chemical analysis showed that this "cell-rich" sweat usually contained 6 to 10 micrograms of iron per cubic centimeter. Duplicate samples were rendered "cell poor" by centrifugation. Analysis showed that most of the "cell-free" samples were iron free. They never contained more than 5 per cent of the iron content of the original opalescent sweat. The conclusion was drawn that iron loss is not an essential function of the sweat glands but is associated primarily with desquamation.

ACTH AND WOUND HEALING

In 1949 Ragan and associates[1] of Columbia University reported a chance observation of delayed healing of wounds in patients treated with pituitary adrenocorticotropic hormone (ACTH). The wounds had occurred as a result of complications unrelated to the basic disease being treated with the hormone. For example, an incised abscess did not form granulation tissue until four days after ACTH therapy had been discontinued. Experimental confirmation of this observation was afterward made on rabbits.[2] Skin wounds were made on both ears of six pairs of adult rabbits. One rabbit of each pair was treated twice daily by intramuscular injections of cortisone acetate, for three days before the wound was made and for five to eight days thereafter, until the time they were killed. The development of granulation tissue was delayed in all of the cortisone-treated animals. At both five and eight days after the operation the treated animals showed practically no granulation tissues. The blood vessels of the wounds were prominent. The control animals revealed good granulation tissues with obscured blood vessels. Histologically the cortisone-treated rabbits showed a striking depression of new growth of all connective tissue elements.

Further confirmations were made by elliptical skin biopsies on patients treated with ACTH.[3] In normal circumstances such wounds should either be healed or show evidence of advanced granulation after one week. Repeated biopsy showed no evidence of healing of the mesenchymal tissues. The wound edges, however, were bridged by a continuous layer of epithelium.

The Columbia surgeons believe that their re-biopsy technic furnished a convenient tool for further study of the mechanism of the therapeutic effects of ACTH and related substances.

"KICKBACKS" CONTRARY TO PUBLIC POLICY

On several occasions comments have appeared in THE JOURNAL on the practice of physicians' receiving "kickbacks" from opticians. The opinions expressed by the House of Delegates and by the Board of Trustees have been reflected in these comments. The practice of "kickbacks" has recently come under the scrutiny of the United States Tax Court. An optical concern, in connection with its federal income tax return, claimed as an ordinary business expense certain amounts returned to physicians whose prescriptions for eye glasses the concern had filled. Apparently these "kickbacks" were made pursuant to agreements or contracts with the prescribing physicians. The claim for deduction was disallowed by the Tax Court principally on the ground that the contracts were considered to be contrary to public policy. "Such a contract," said the court, "is contrary to public policy, inasmuch as the relationship involved between the parties is not that of an ordinary commercial transaction. The relationship here is between doctors and their patients, and there is no doubt of the exceedingly high degree of confidence and trust inherent in that relationship. Although there is no constitutional provision condemning the practice or statutory provision denying the deduction, the doctor cannot at the same time 'serve two incompatible masters.' Since the contracts are void, the payments made under them are not deductible as ordinary and necessary expenses."[1]

1. Mitchell, H. M., and Hamilton, I. S.: J. Biol. Chem. **178**: 345, 1949.
2. Adams, W. S.; Leslie, A., and Levin, M. H.: Proc. Soc. Exper. Biol. & Med. **74**: 46 (May) 1950.
3. Leslie, A., and Levin, M.: Am. J. Med., to be published.

1. Ragan, C.; Grokoest, A. W., and Boots, R. H.: Am. J. Med. **7**: 741, 1949.
2. Ragan, C.; Howes, E. L.; Plotz, C. M.; Meyer, K., and Blunt, J. W.: Proc. Soc. Exper. Biol. & Med. **72**: 718, 1949.
3. Creditor, M. C.; Bevans, M.; Munchy, W. L., and Ragan, C.: Proc. Soc. Exper. Biol. & Med. **74**: 245 (May) 1950.

1. *Thomas B. Lilly v. Commissioner, Helen W. Lilly v. Commissioner*, Dkts. 18881, 18882, June 6, 1950, 14 TC—, No. 120, opinion by Judge Leech.

WASHINGTON NEWS

(From the American Medical Association Washington Office)

Hearings on Draft Legislation

Senate hearings on doctor-draft legislation (S. 4029) confirmed that the general purpose of the bill had widespread support but that important differences of opinion existed on details. Furthermore, witnesses were far from agreement on how physicians should be apportioned on a civilian-military basis, as well as on the question of what federal agency if any should be given authority to enforce allocation.

The bill under discussion, like a number of House bills on the same subject, provided for drafting of physicians by categories, with former ASTP and V-12 students scheduled for first induction calls. It provoked discussion of the broader issue of civilian versus military requirements because it proposed a National Specialists Category Advisory Board to advise in selection of physicians for military service. One question was whether this advisory board should concern itself with civilian-military allocations or whether another body with greater authority should be created for this purpose.

Dr. Walter B. Martin, A.M.A. Trustee, told the Committee: "It is our understanding that the National Security Resources Board now has the responsibility of considering requirements of the armed services for specialist personnel to assure an equitable distribution of such personnel between the armed services and the civilian population. We are recommending that special mention be made in this bill of the relationship between NSRB and other federal agencies, but the committee may wish to insert some statement underlining the fundamental responsibility of NSRB in connection with this special registration and call-up of specialists."

Dr. Martin, recognizing that NSRB was created and functions in an advisory capacity only, pointed out that there should be some balance between military and civilian medical service. Dr. Elmer L. Henderson, A. M. A. President, and Dr. James C. Sargent, chairman of A. M. A.'s Council on National Emergency Medical Service, agreed with Dr. Martin on this point, but none proposed that NSRB be given allocation authority. All suggested instead that NSRB, the military services and Selective Service cooperate to solve the problem.

Dr. Leonard A. Scheele, Public Health Service Surgeon General, suggested state quotas for physicians but advised against creation of a national advisory board and urged that no one agency be given allocation authority at the present time. He said:

"The Nationwide allocation of physicians and dentists for military and various civilian purposes is clearly a problem for the highest levels of government. There is certainly need for careful consideration and advice on these matters by an advisory body broadly representative of the various professional groups, including hospital and public health interests, and—very important—the general public, which is, after all, the consumer of health services. It is perhaps unwise to freeze by legislation at this time the type and location of such an advisory body; it seems to be preferable simply to recognize the overriding responsibility of the President, who already has available a statutory advisory body which is concerned, among other things, with manpower allocation, namely the National Security Resources Board."

However, at the same hearing, the president of the American Dental Association flatly called for elevation of NSRB to an operating status, with full authority to apportion physicians and dentists between civilian and military populations. Speaking for A.D.A., Dr. Philip E. Adams declared:

"The association realizes that the National Security Resources Board at the present time is a planning and not an operating agency. It also realizes that NSRB has recently established the office of Health Resources which incorporates divisions of NSRB which prior to that time had been engaged in studying the health problems of the nation and more particularly the manpower and civilian defense needs in this field.

"The Association believes that this office can readily be converted to an operational status and that with its present information and resources plus the assistance of the advisory committees proposed it can function effectively to prevent some of the fiascos of the last war and to insure a steady supply of trained professional manpower for both the Armed Services and the civilian economy."

Other officials and agencies heard by the Senate Committee included NSRB, Selective Service, Dr. Richard Meiling, head of the Defense Department's Office of Medical Services, and the three Surgeons General. Senator Lester C. Hunt (Democrat, Wyoming), chairman of the subcommittee which took the testimony, indicated he was determined to get a doctor-draft bill passed before Congress recesses.

Until this law becomes effective, military services will have to continue calling up medical reserves at the rate of more than 100 a week. Once the bill is signed by the President, the services will start to call up physicians who have had little or no active duty. Available for service, under the law, will be about 6,000 former ASTP and V-12 men, plus a few hundred others who did not see service in World War II.

Action of Committee on Medical Care for Veterans' Dependents

A move to extend military medical care to dependents of all enlisted men was slowed down by action of the House Armed Services Committee, which declined to include this provision in the bill granting financial allowances to such dependents. The Committee acted despite recommendation of a subcommittee that these dependents be cared for "wherever practicable." Testifying for the A. M. A. before the subcommittee, Dr. Martin pointed out objections to the bill. He said the A. M. A. agreed that outside the Continental limits, and in certain circumstances within these limits, it may be desirable to provide such medical and hospital care. Dr. Martin added, "It is our understanding that this is already being done and that it is being accomplished under the present law." Dr. Martin then listed seven objections:

1. Only a small fraction of otherwise eligible dependents would have ready access to military hospitals because of geographic factors; discrimination would result.

2. The bill's language ("hospital and medical care") was too indefinite for practical interpretation.

3. If the language is interpreted broadly and taken advantage of on a large scale, hospital and medical facilities of the Armed Forces will be overburdened, new facilities required.

4. If this occurs, large numbers of additional military physicians and enlisted personnel will have to be obtained.

5. Military medical departments might be diverted from their primary mission of supporting our defense to the "less important purpose" of providing for dependent civilians.

6. Medical and hospital care could be provided for these dependents more readily, more cheaply and more effectively through existing civilian facilities.

7. It would deplete civilian medical personnel and civilian hospitals, often diverting patients from local hospitals to remote service hospitals.

Subsequently the committee was informed by a Defense Department spokesman that the military services already had the authority to extend medical care to dependents of enlisted personnel. In view of this, and the rush toward a recess, it was considered unlikely that this bill would pass.

Better Use of Medical Personnel

The Army has announced a new policy aimed at better utilization of medical personnel, which it hopes will remove some of the major causes of complaint among medical officers in World War II. During the last war, doctors often were held in pools for long periods of time awaiting assignment.

The Army's attempt to achieve better distribution affects two groups:

1. Army divisions, headquarters of medical battalions and groups, medical clearing companies, medical field laboratories, field hospitals, mobile Army surgical hospitals and all non-medical units with medical personnel included in their organization.

2. Evacuation hospitals, convalescent centers, general and station hospitals, general laboratories, hospital trains and general dispensaries.

The policy for the first group will be to call all officers with their units but assign only a minimum number to train with the units and assign the remaining officers to the hospital serving the division. By rotating these physicians the Army hopes to assure a balanced program. The Army gives this example: An infantry division is authorized 42 physicians, but only 17 would be retained during the training period, with the rest assigned to the hospital serving the division.

In the second group, only those doctors actually required for training will be called under the new policy. The rest would remain at home until shortly before the unit is actually ready for operation. The Army's example here is a 1,000 bed general hospital where only three doctors will be required when the unit is called. The rest of the physicians with that unit would not be called until the unit went into action.

NOTE.—All Medical Service Corps officers attached to organized units will be called to active duty with their units.

Propaganda for Compulsory Health Insurance

New ammunition has been thrown into the campaign to promote national compulsory health insurance. The latest effort from the Democratic National Committee is a handbook for party workers, devoted solely to President Truman's health plan. It is designed to supplement a smaller, mass appeal pamphlet, "Better Medical Care Than You Can Afford," already circulating in the hundreds of thousands. The latest booklet, "Administration Health Program—A Training Kit for Leaders," is directed toward group leaders and those engaged in campaign publicity work. For their convenience, it contains quotations, extracts from reports and a fair amount of statistical data. Although the material is mostly the familiar mixture of information and propaganda, it is well arranged for fast reference. The 80 pages are broken up by sections, headings and bold face type. An index, résumé and cross reference system are provided. One entire section is devoted to activities of the opposition. This is a 17-page attack on the A. M. A., usually referred to as "Organized Medicine." Included are 36 questions, such as "Is it true that America has 'low grade' health care?" Answers are printed in parallel columns under the headings "Lobbyists Say" and "The Truth Is."

The last chapter is devoted to advice on how best to appeal to special population groups, such as housewives, farmers, industrial workers, Negroes and businessmen. One section tells party workers what arguments to use when they attempt to convince doctors that national health insurance would be to their advantage. (Any inquiries about this book should be addressed to Democratic National Committee, Ring Building, Washington, D. C.).

Military Notes

If an Army medical reserve officer wants to volunteer, "generous consideration" will be given to the question of waving physical requirements. . . . Fifty veterinarians, not 92 as previously announced, are being called up. . . . So far there is no over-all Army policy covering such questions as whether the reserve in an office position should be called up ahead of a man in practice. . . . Former ASTP and V-12 physicians are eligible for Air Force commissions if they have no commission in another branch of service. Men volunteering with the Air Force also receive the $100 bonus. . . . Fort Sam Houston, Texas, has been activated as a medical replacement training center. In addition to facilities for 15,000 enlisted men, six-week orientation courses for reserve officers with no previous active duty and civilian intern trainees are being given. . . . Bills for Universal Military Training do not change that status of medical students. As at present under Selective Service medical students could be deferred at the discretion of the local boards. . . . The Army is now commissioning women physicians in the Medical Department. However, they have to agree to go on active duty concurrently with receipt of their commissions.

H. R. 9501

In a long range attempt to provide more military doctors, Representative James B. Hare (Democrat, South Carolina) proposes to grant federal scholarships in return for active duty. His bill (H. R. 9501) would allow qualified students $75 per month in addition to tuition and other school costs. On graduation, the doctor would be obligated for a period of active duty equal to the time spent in medical school. The bill places no limit on the number of students who might be assisted at any time. The Army itself is making another short range effort to solve the problem. It is offering contracts to civilian physicians for service in Japan and Okinawa. Salary ranges between a minimum of $6,400 in Japan to a maximum of $11,000 in Okinawa. An appeal is being made to physicians seeking "broad medical experience with unlimited clinical material," as well as to pediatricians, roentgenologists, obstetricians, gynecologists and urologists. The Army also has closed its hospitals to additional VA cases, except in emergencies, and the Defense Department announced that the Navy will have to adopt the same rule.

Agencies

The Food and Drug Administration has authorized dentocillin,® first toothpowder containing penicillin, for sale on prescription only. Dr. Helmut A. Zander, professor of dentistry at Tufts College, developed the powder, which reduced caries rates by 55 per cent in clinical tests. . . . Robert A. Statler has been appointed chief of the training section of VA's pharmacy division in Washington, D. C. . . . Although Public Health Service closed down its Division of Federal Employee Health last June, PHS has completed a study among 3,425 federal employees in Denver to determine the effect of preventive health programs on sick leave. PHS conclusions show an average reduction of six hours sick leave per person per year. Although the program cost $38,000, it resulted in a saving of $32,880. PHS feels that with certain improvements it could pay for itself. PHS no longer operates federal employee health programs but can cooperate with any agency setting one up.

Aid to Medical Education

Also basing his action on the emergency situation, Representative Andrew Biemiller (Democrat, Wisconsin) has introduced still another bill on federal aid to medical education. The House Interstate and Foreign Commerce Committee has voted down this legislation twice this session, but by one vote margins. Members said the last vote was influenced by the fact that this legislation would not produce more doctors for several years.

GOVERNMENT SERVICES

Army

Recall of Reserve and National Guard Officers

Since the announcement of the Army of its initial call for 734 medical reserve officers, the Surgeon General has been receiving an increasing number of inquiries. On request from the editor of THE JOURNAL, typical questions and replies have been prepared for the readers of THE JOURNAL on the basis of information supplied by the Surgeon General's Office. The answers reflect the policies that the current military and national situation dictates. "Delays" refer to postponement of service for six months or less under the policy of the Secretary of Defense. "Deferments" refer to postponement of service under the Selective Service System.

Q. *Is a National Guard or Army reserve officer or enlisted man who is a premedical student eligible for delay under the policy of the Department of Defense?*

A. Under announced policies of the Department of Defense, call to active duty of a member of the civilian components enrolled in an educational institution may be initially delayed until completion of the school term in which the member is then registered. At the end of the initial specified delay, extension of delay may be requested. The established policy does not permit blanket deferments. Each case must be considered and acted on separately.

Q. *Is the premedical student who is not a member of the reserve or National Guard eligible for deferment from the draft?*

A. Announcements of policy by the National Headquarters, Selective Service System, should be consulted in connection with this question. The National Headquarters, Selective Service System, issued, on Nov. 2, 1948, Local Board Memorandum 7, subject: "Students of Healing Arts." Provisions are contained therein for deferment of certain preprofessional students (including medical) who have successfully completed at least one year of preprofessional study and have been provisionally accepted for entrance into the professional school.

Q. *Is a National Guard or Army reserve officer or enlisted man who is a medical student or intern eligible for delay from call to active duty?*

A. Graduates of advanced course senior division ROTC and members of civilian components enrolled, or who have been accepted for admission, in a recognized school of medicine will be delayed in call to active duty until the end of the fall quarter or semester of their college or university. At the end of the initial specified delay, extension may be requested. Members of civilian components who have not completed at least one year of intern training will also be granted delay in call until completion of one year's internship.

Q. *Is a medical student, intern or resident who is not a member of the reserve or National Guard eligible for deferment from the draft?*

A. Announcements of policy by the National Headquarters, Selective Service System, should be consulted in connection with this question. Provisions for permitting students who are not otherwise deferrable under the Selective Service Act of 1948, as amended, and who are properly enrolled in certain professional schools (including schools of medicine) and satisfactorily pursuing full time courses leading to graduation, to continue their studies until graduation are contained in Local Board Memorandum 7.

Q. *Is a National Guard or Army reserve officer or enlisted man who is in residency training eligible for delay?*

A. Only those in the last year of their residency are eligible for initial delay. Enlisted men of the civilian components in this category are urged to apply for appointment in the Medical Corps Section of the Officers' Reserve Corps under the provisions of Department of the Army Circular 210 of 1948, or to the State Adjutant General of the state of their residence, for appointment as a medical officer in the National Guard.

Q. *What actions should be taken by those medical students who are members of line organizations in the National Guard or reserve?*

A. Medical students who are commissioned or enlisted in the reserve should notify, through their appropriate channel, the chief of their military district as to their status as medical students, if such information is not already, to their knowledge, a matter of official record. In the event of their call to active duty, they may request a delay in such call under the announced policies of the Department of the Army. Those officers of the reserve who are qualified for transfer to any one of the Corps of the Army Medical Service Reserve may submit a request for transfer under the provisions of SR 140-160-1. Such request should be submitted through appropriate reserve channels to the Commanding General of the Army in whose area they reside. Persons enlisted in the reserve who are qualified for appointment in any one of the Corps of the Army Medical Service Reserve may apply for appointment under the provisions of Department of the Army Circular 210 of 1948. Medical students enlisted or commissioned in the National Guard are under the jurisdiction of the State Adjutant General concerned prior to their induction. Requests for determination of status, commissioning or transfer to the Medical Corps and granting of any delay in call to duty of such persons should be directed to the State Adjutant General concerned.

Q. *What action should be taken by interns and residents who are members of line organizations in the National Guard or reserve?*

A. Those officers of the reserve who are qualified for transfer to any one of the Corps of the Army Medical Service Reserve, may submit a request for transfer under the provisions of SR 140-160-1. Such request should be submitted through appropriate reserve channels to the Commanding General of the Army in whose area they reside. Persons enlisted in the reserve who are qualified for appointment in any one of the Corps of the Army Medical Service Reserve may apply for appointment under the provisions of Department of the Army Circular 210 of 1948. Medical students enlisted or commissioned in the National Guard are under the jurisdiction of the State Adjutant General concerned prior to their induction. Requests for determination of status, commissioning or transfer to the Medical Corps, and granting of any delay in call to duty of such person should be directed to the State Adjutant General concerned.

Q. *What obligation is incurred by a person accepting a delay or deferment?*

A. No additional obligation is incurred by reason of acceptance of a delay in call to duty or deferment. On termination of such delay or deferment the person is subject to call to active duty on the same basis and under the same procedures as he would have been initially called.

Q. *What other individual reserve or National Guard medical officers are eligible for consideration for delay from call to duty?*

A. 1. Reserve medical officers *now* pursuing a full time postgraduate course of instruction in medicine, at a college, university or similar institution of higher learning until completion of the current academic year of such training.

2. Reserve medical officers whose activity in teaching, research and allied endeavors is considered by the appropriate Army Commander to be essential to the national health, safety or interest.

3. Reserve medical officers residing in communities the health of which, in the opinion of the appropriate Army Commander, would be unduly jeopardized if such officers were to be ordered to extended active duty.

Q. *How, when and to whom should requests for delay be submitted?*

A. Requests for delay in call to active duty should be submitted in writing on initial receipt of notification that call to active duty is contemplated. For members of the reserve, such requests should be submitted to the headquarters responsible for the issuance of the notification, as authority has been granted by the Department of the Army to such headquarters to take appropriate action. Redelegation of this authority may be made by those commanders to subordinate headquarters commanded by a general officer or to a Chief of Military District. Only those requests that cannot be determined at Army Commander level will be forwarded to the Department of the Army (The Adjutant General, Attn: AGAO-C) for final appeal. In the case of National Guard personnel, requests for delay should be forwarded to the State Adjutant General.

Q. *Will medical units be brought to duty for training periods with their full complement of physicians and nurses?*

A. In order to assure that physicians and nurses are effectively utilized within the Department of the Army, only certain types of organizations will be brought to active duty with their full complement of such personnel. These types are as follows:

Infantry Division
Armored Division
Airborne Division
Hq and Hq Det, Med Bn, Sep
Hq and Hq Det, Med Gp
Medical Clearing Company, Sep
Medical Field Laboratory, Army
Field Hospital
Mobile Army Surgical Hospital
All nonmedical units with medical personnel included in its T/O

Other types of medical units, such as those reflected below, will not be brought to active duty with their full complements of physicians and nurses, but with the number considered necessary for effective training. Additional personnel will be ordered to active duty at such time as the unit is to become operational.

Evacuation Hospital, Semimobile
Evacuation Hospital (750 patient)
Convalescent Center, Army
General Hospital, 1,000 bed
Station Hospital, 500 bed
Station Hospital, 300 bed
Station Hospital, 200 bed
Station Hospital, 100 bed
General Laboratory
Hospital Train
General Dispensary (MB)

Q. *May members of organized reserve and National Guard units expect to remain together throughout their service?*

A. It is the policy of the Army to maintain the integrity of the unit wherever possible. However, maximum and efficient utilization of personnel may make it necessary in some cases to reassign certain individuals. Unnecessary reassignment of personnel will not be made.

Q. *Are members of the inactive and honorary reserve eligible for call?*

A. Officers in the inactive reserve are subject to call to active duty on the same basis as officers in the active reserve. Officers in the honorary reserve may be called to active duty only with their consent.

Q. *Is there an immediate need for senior medical officers?*

A. No, except for certain specialties:

Military Occupational Specialty Number	Specialty
3000 or 3500	Staff or Command
3005	Preventive Medicine
3101	Tuberculosis
3129 and/or 3130	Psychiatry
3139	Internal Medicine
3150	General Surgery
3303 and/or 3325	Medical Laboratory or Pathology

Q. *Will reserve officers with long periods of active military service be given consideration in call to active duty?*

A. Present policies of the Department of the Army require that individual selection of officers of the Medical Corps Reserve for active duty be made, whenever feasible, from among those with no previous active military service, followed by officers with less than one year of extended active duty, and so forth. In the case of persons who are members of units ordered to active duty, if the individual officer feels that his circumstances justify a delay in call to active duty, necessary request in writing should be submitted through his Commanding Officer to the headquarters authorized to take action on such requests.

Q. *Is any effort being made to obtain services of former ASTP participants and those who did not serve during last war?*

A. Legislation has been introduced in the present session of Congress which, if enacted into law, will require military service of those persons who received a portion, or all, of their medical education under the Army Specialized Training Program or the Navy V-12 Program and who have not served in the armed forces subsequent to completion of their medical education. It is important, however, to realize that the successful implementation of any legislation of this nature will require a lapse of some months. As an example, nationwide registration of persons of any category embraced in any legislation, under conditions as might be prescribed therein, will, in itself, be a necessary but time-consuming preliminary.

Q. *How have quotas for recalls been allocated to Army areas?*

A. Quotas for recall to active duty of individual reserve Medical Corps officers have been allocated by grade and military occupational specialty on the basis of number of physicians to population in each Army area.

Q. *In what grade will reserve officers be recalled?*

A. Reserve officers, irrespective of whether called to active duty voluntarily or involuntarily, will be called in the grade in which they are currently commissioned in the Officers' Reserve Corps.

Q. *Who is entitled to additional professional pay?*

A. It is the opinion of the Surgeon General, Department of the Army, that, prior to the issuance of orders calling him to active duty, any medical or dental officer of the ORC or National Guard who volunteers for, and is accepted for, extended active duty for a period of at least 21 months is entitled to be classified as a volunteer under the provisions of Section 203 of the Career Compensation Act of 1949 and to receive additional special pay of $100 per month. This opinion is subject to the confirmation of the Comptroller General.

Navy

General Policies and Procedures

The following statement was made by Rear Admiral A. H. Dearing, Assistant Chief, Bureau for Personnel and Professional Operations, Bureau of Medicine and Surgery, Department of the Navy, before the Joint Committee on Medical Education in Time of National Emergency, Aug. 11, 1950, Washington, D. C. Numerous inquiries are being received in the Bureau of Medicine and Surgery concerning these matters.

1. Action on requests for deferment or delay in call to active duty from members of the reserve components of the Armed Forces is governed by a statement of policy issued by the Secretary of Defense on Aug. 1, 1950, and the implementing directives issued by the Chief of Naval Personnel and the Commandant of the Marine Corps.

2. The established policy does not permit blanket deferment for any particular group or category of individuals. Each case must be considered and acted on separately.

3. Advance deferment or delay in call to active duty is not authorized. Requests for deferment or delay should not be submitted until orders to report for active duty have actually been received.

4. Deferments may not be granted for more than six months but may be granted for shorter periods. At the end of the deferment period, request for further deferment may be submitted. Medical students who are members of the Naval or Marine Corps Reserve, in other than Ensign HP classification, should apply for change in status to Ensign HP during the first period of deferment.

5. Medical students, interns, residents and medical officers who are members of the Naval or Marine Corps reserve and who desire deferment or delay in call to active duty should, within 48 hours after receipt of orders, apply for deferment or delay to the authority issuing the orders, via the channels through which the orders were received.

6. In the mobilization plans of the Department of the Navy, the Organized Reservist is considered to be available for immediate mobilization and the Volunteer Reservist within a maximum period of 30 days. The Organized Reserve medical personnel are those individuals who have been trained, who have attended weekly drills and been paid therefor, and have also been paid for 14 days training duty each year. On assignment to the Organized Reserve they are required to sign an affidavit that they are available for immediate mobilization and that they will notify their commanding officer of any change in their civilian status which would make it impossible for them to be immediately available for active duty.

The Volunteer Reserve personnel, on the other hand, do not subscribe to such an affidavit and receive no pay except for such short periods of training as they may volunteer for.

7. In considering requests of Organized Reservists, an effort will be made to defer residents and others so long as military necessity permits. However, it is our firm feeling that individuals in the Organized Reserve should *not* be deferred to an extent which would necessitate the call to active duty of Volunteer Reservists, except for the most urgent reasons. Each case will be referred to the Bureau of Medicine and Surgery where it will be reviewed by a Board convened for this purpose. This Board will make its recommendation in each case to the Deferment Board in the Bureau of Naval Personnel. Final decision in each case rests with the Chief of Naval Personnel.

MEDICAL STUDENTS

1. It is not intended that medical students who continue in good standing and obtain change in classification to Ensign HP in the Naval Reserve shall be called to active duty prior to graduation from medical school.

2. All medical students in good standing and persons who have been accepted for the next entering class are eligible to apply for commission as Ensign HP, USNR. Full information and assistance in the preparation and submission of an application may be obtained at the nearest Office of Naval Officer Procurement.

Medical students who hold commissions in the Naval Reserve in other than the Ensign HP classification who receive orders to active duty and apply for deferment should at the same time apply to the Bureau of Naval Personnel for change in status to Ensign HP.

3. Medical students who are enlisted members of the Naval Reserve or commissioned or enlisted members of the Marine Corps Reserve, who receive orders to active duty and apply for deferment, should immediately apply at the nearest Office of Naval Officer Procurement for commission as Ensign HP in the Naval Reserve.

INTERNS

1. It is not the intent to call to active duty interns holding commissions in the Medical Corps until the end of their present intern year. It is desired that interns be allowed to complete at least twelve months of internship.

2. Interns holding commissions in other than the Medical Corps, or holding enlisted ratings, should make immediate application at the nearest Office of Naval Officer Procurement for commissions in the Medical Corps Reserve unless it is their desire to serve on active duty in their present reserve status.

3. Interns who have no reserve status are also eligible to apply at the nearest Office of Naval Officer Procurement for commission as lieutenant (junior grade) in the Medical Corps of the Naval Reserve.

RESIDENTS

1. The Bureau of Medicine and Surgery and the Bureau of Naval Personnel fully appreciate the desirability of allowing residents to complete as much training as possible. However, military necessity and the status of the officer within the Reserve structure must be taken into consideration in acting on requests for deferment or delay. It is the feeling in the Navy Department that those in the Organized Reserve should be called to duty before those in the Volunteer Reserve.

2. Residents who hold commissions in other than the Medical Corps of the Naval Reserve or who hold enlisted ratings in any classification should make immediate application at the nearest Office of Naval Officer Procurement for a commission in the Medical Corps of the Naval Reserve.

3. Residents who have no reserve status may also apply at the nearest Office of Naval Officer Procurement for a commission in the Medical Corps of the Naval Reserve.

Addendum to Statement of Rear Admiral A. H. Dearing.

The Chief of Naval Personnel has concurred with the views and comments of the Bureau of Medicine and Surgery with regard to the deferment policy applicable to medical students holding reserve commissions or ratings. The following abstract from a letter from the Chief of Naval Personnel to the Chief of the Bureau of Medicine and Surgery, dated 14 August 1950, is quoted for information:

"(*a*) It is understood that the terms 'Medical Students' and 'Dental Students' include personnel who are enrolled in, or have been accepted for the next entering class, an accredited Medical or Dental School. These terms do not pertain to undergraduates pursuing pre-medical or pre-dental studies who, under the provisions of the Department of Defense Occupational Deferment Policy, are eligible for delay in call to active duty only until completion of the school term in which registered.

"(*b*) The Chief of Naval Personnel considers it improper for medical and dental students to participate in the Organized Reserve unless the training received therein is to be utilized upon their call to active duty. It must be assumed that medical and dental students who continue to participate, in lieu of requesting a change in status to Ensign H(P), do so with the desire to serve on active duty in other than medical or dental assignments. Further, these members are aware that large numbers of personnel of the Organized Reserve have been called involuntarily and further recalls are imminent. The above assumption is likewise applicable to members of the Volunteer Reserve who fail to request a change in status. While the rate of recall is not high at present, members of the Volunteer Reserve are being called involuntarily.

"(*c*) In view of the above considerations, the procedure whereby medical and dental students may change their status to Ensign H(P) will be brought again to the attention of such personnel. They will be informed that members who decline to change their status will not be granted a delay in call to active duty because of their status as medical or dental students.

"(*d*) ONOP's (Offices of Naval Officer Procurement) will be informed that for the time being there is no restriction on the procurement of Ensigns H(P)."

Air Force

Air Force Seeks ASTP and V-12 Trained Physicians

Physicians who received all or part of their training under the Army Specialized Training Program (ASTP) or the Navy V-12 Program and who do not have commissions with other military services are eligible to receive commissions in the U. S. Air Force Medical Service, Major Gen. Harry G. Armstrong, Surgeon General, U. S. Air Force, announced. The present law provides that physicians who volunteer for service will receive an extra $100 a month in addition to regular pay and allowances. They will be commissioned as first lieutenants unless their professional qualifications entitle them to a higher rank. Information may be obtained on written request from the Surgeon General, Headquarters, U. S. Air Force, Washington 25, D. C., or from the nearest Air Force base.

Public Health Service

Construction Projects for Hospitals

The Public Health Service by June 30, 1950, approved a total of 1,367 construction projects for hospitals and health centers under the Hospital Survey and Construction Act. Hospital additions and new hospitals accounted for 1,123 projects, and the remaining 244 construction projects were for health centers. The estimated cost of the projects is over $952 million, of which over $344 million will come from federal funds.

The 1,123 hospital construction projects that have been approved thus far would provide 65,542 additional hospital beds. The majority of these beds, 51,651, are in general hospitals. In addition, the construction projects would provide 6,555 hospital beds in mental hospitals, 4,527 beds in tuberculosis hospitals and 2,809 beds for the chronically ill.

The accompanying tables show the states and territories with the largest number of hospital construction projects, those with the largest number of beds to be added and those with the largest number of health centers.

States with 50 or More Approved Hospital Projects

Texas	80
Mississippi	58
North Carolina	58
New York	53

States Adding More Than 2,500 Hospital Beds

Texas	5,117
New York	3,185
Pennsylvania	2,988
Ohio	2,946
North Carolina	2,922
Mississippi	2,689
Kentucky	2,572

States with 10 or More Approved Health Center Projects

South Carolina	60
Mississippi	44
Georgia	29
Louisiana	19
Ohio	11

Students from Okinawa and Japan

Several physicians and other health workers have arrived from Okinawa and Japan for three months' training in the United States under programs supervised by the Division of International Health. The training is being conducted under a fellowship plan established by the Military Government of Japan.

The physicians from Okinawa, their affiliation, and field of study are:

Dr. Zenshi Inafuku, Okinawa Central Hospital, laboratory and hospital administration.

Dr. Shinken Ohama, president, Yaeyama Doctor's Association, public health administration.

The physicians from Japan are:

Dr. Yoichi Azuma, director, Japanese Red Cross Central Hospital, Tokyo, surgery and hospital administration.

Dr. Kikuo Hamano, in private practice in Chiba prefecture, the role of the private practitioner in health services of rural and urban communities.

Dr. Tatsuo Kariyone, Professor, Kyoto National University, Kyoto, and President of the Pharmaceutical Association of Japan, pharmaceutical practice and its relation to other medical professions.

Dr. Toyokiro Kato, chief, Sendai National Hospital, Sendai, advances in internal medicine.

Dr. Rokuzo Kobayashi, director, National Institute of Health, Tokyo, laboratory administration and preparation of biologicals.

Dr. Yoshiatsu Ozaki, Chief of Food Santitation Section, Public Health Bureau, Ministry of Welfare, Tokyo, public health administration and food sanitation.

Appoint Chief of Blood Products Section

Dr. John T. Tripp has been appointed chief of the Section on Human Blood Products in the Laboratory of Biologics Control of the Microbiology Institute. The section establishes standards for the production, testing and sterilization of whole blood, plasma and other blood products in licensed laboratories as provided by the federal biologics law. Dr. Tripp was formerly assistant director of the Division of Laboratories of the Michigan Department of Health, where he was in charge of the manufacture of serums and vaccines.

Miscellaneous

Advisory Committee for Biology and Medicine

Dr. Edward A. Doisy of St. Louis and Dr. Curt Stern of Berkeley, Calif., have been appointed to the Atomic Energy Commission Advisory Committee for Biology and Medicine. Dr. Doisy, a native of Illinois, received a B.A. degree from the University of Illinois in 1914 and Master of Science degree in 1916 and a Doctor of Philosophy in biochemistry from Harvard University in 1920. For many years he has been professor in the School of Medicine at St. Louis University and director of the Department of Biochemistry. During the war he was with the Office of Scientific Research and Development. He was co-winner of the Nobel prize for Medicine in 1943. Among his primary scientific interests have been studies of metabolism, hormones and estrogenic substances, and antibiotic substances.

Dr. Stern, born in Hamburg, Germany, became a naturalized United States citizen in 1939. He obtained the degree of Doctor of Philosophy in zoology from the University of Berlin in 1923 and for 10 years was at the Kaiser Wilhelm Institute as investigator and privatdocent. From 1933 to 1947 he was professor of zoology at the University of Rochester, Rochester, N. Y., and from 1941 was chairman of the Division of Biological Sciences. Since 1947 he has been professor of zoology at the University of California. He has been particularly interested in human and general genetics and cytology.

The other members of the Advisory Committee for Biology and Medicine include Dr. Alan Gregg, chairman, director for medical sciences, Rockefeller Foundation; Dr. Detlev W. Bronk, president, Johns Hopkins University; Dr. Ernest W. Goodpasture, dean of the school of medicine, Vanderbilt University; Dr. E. C. Stakman, chief, division of plant pathology and botany, University of Minnesota, and Dr. Joseph T. Wearn, dean of the school of medicine, Western Reserve University.

Red Cross to Administer Atomic Energy Blood Separation Research

Improved methods for separating and preserving blood components of interest in atomic energy research will be sought in a program administered by the American National Red Cross under a contract with the Atomic Energy Commission. The primary interest of the AEC in blood fractionation studies is the development of means for separation and preservation of white blood cells and platelets, which are two blood components of particular value in combating acute radiation effects. In its initial studies under the contract, however, the Red Cross will administer engineering development of new and quicker methods for obtaining and preserving plasma and red blood cells. In connection with civil defense planning there is an acute need for development of facilities that can separate quickly large quantities of blood fractions so that stockpiles of blood constituents will be available in the event of atomic disaster.

None of the AEC funds will be used to finance central overhead or operating expenses of the Red Cross National Blood Program, nor does the contract provide for establishing blood banks. The following technical personnel will be engaged in AEC blood fractionation research under the administration of the Red Cross: Boston, Drs. J. G. Gibson III, C. B. Favour, James Tullis, Reginald Kernan, Ben Alexander, Charles Emerson, F. Gardner, E. Twible, N. N. Smith and Louis K. Diamond; Chapel Hill, N. C., Dr. Kenneth M. Brinkhous; Chicago, Dr. Henry Poncher; Columbus, Drs. Charles A. Doan and Warren Wheeler; Durham, N. C., Dr. Ivan W. Brown; New York, Drs. Allen A. Minor and Aaron Kellner; Philadelphia, Dr. I. S. Ravdin; Richmond, Dr. Everett I. Evans; St. Louis, Dr. Carl V. Moore, and San Francisco, Drs. Paul Aggeler and Robert Evans.

MEDICAL NEWS

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

ALABAMA

Appoint Professor and Acting Dean.—Dr. Tinsley R. Harrison, Nashville, Tenn., has been appointed professor of medicine and acting dean at the Medical College of Alabama, Birmingham. As professor he will fill the vacancy made by the retirement last year of Dr. John S. McLester, and as acting dean he will carry on the work of the late Dr. Roy R. Kracke. Dr. Harrison was at one time dean as well as professor of medicine at Southwestern Medical College in Dallas, Texas. He moved to Nashville to take up private practice in 1949. He had previously been on the faculty of Vanderbilt University School of Medicine and Bowman Gray School of Medicine of Wake Forest College. Two years ago he was president of the American Heart Association.

CALIFORNIA

Society News.—The California Society of Internal Medicine will hold its first annual scientific-social meeting in Yosemite September 23-24 with headquarters at the Ahwahnee Hotel. The scientific program will be held on Saturday morning. Dr. John S. Browne, professor of medicine at McGill University Faculty of Medicine, Montreal, Canada, will be the principal speaker. Dr. Browne, who has done some of the original work on pituitary adrenocorticotropic hormone (ACTH), will conduct a symposium on recent developments and experiences with cortisone and ACTH. The dinner will be held Saturday evening.

Course in Care of Poliomyelitis Patients.—Beginning October 9 a four day course in care of the poliomyelitis patient is being offered for physicians by Orthopaedic Hospital, Los Angeles, with aid from the National Foundation for Infantile Paralysis. Latest developments in respirator technics and care during the acute stage will be presented through cooperation with Los Angeles County General Hospital. Postacute treatment will be presented with emphasis given to coordination of services. For information address C. L. Lowman, M.D., Director of Education and Rehabilitation, 2400 South Flower Street, Los Angeles 7.

GEORGIA

Associate Deans at Emory.—Dr. Paul B. Beeson and Dr. Arthur P. Richardson, Atlanta, who are Emory University professors, have been appointed associate deans of the medical school to assist Dr. R. Hugh Wood, dean. Dr. Beeson is chairman of the department of medicine, and Dr. Richardson, chairman of the department of pharmacology.

State Heart Association.—The Georgia Heart Association will hold its annual meeting September 15-16 in conjunction with the annual meeting of the Fifth District Medical Society at the Academy of Medicine and the Biltmore Hotel in Atlanta. The guest speakers and their topics will be:

Tinsley R. Harrison, Birmingham, Ala., Unusual Aspects of Chest Pain.
James A. Shannon, Bethesda, Md., Trends in Cardiovascular Research.
John P. Merrill, Boston, Role of the Artificial Kidney in Cardiovascular Diseases.
Edgar Hull, New Orleans, Choice of Leads in Clinical Electrocardiography.
Eugene B. Ferris, Cincinnati, Diagnosis and Management of Hypertension.

In a round table, "The Layman Looks at Heart Disease," outstanding leaders in the fields of education, agriculture, industry, labor and civic affairs will pose questions to the visiting speakers.

ILLINOIS

County Hospital Dedicated.—Dedication ceremonies of the Lawrence County Memorial Hospital at Lawrenceville were held July 2, when about 7,000 persons inspected the new building after the ceremonies. This 50 bed hospital will also house the offices of the county health department and the county tuberculosis sanatorium board. The building was erected with state and federal aid at a cost of nearly a million dollars.

Chicago

Death of Mr. Stack.—Alfred W. Stack, aged 60, director of fellowship and membership records and director of circulation of THE JOURNAL and the specialty journals published by the American Medical Association, died August 4 after a short illness. Mr. Stack joined the American Medical Association staff on April 1, 1924, as assistant circulation manager. He also managed the registration work at the American Medical Association meetings. The thousands who knew him cherished his kindliness and friendship.

Televised Conference on Obstetrics and Gynecology.—The department of obstetrics and gynecology of the Stritch School of Medicine, Loyola University, will present its second televised Postgraduate Conference in Obstetrics and Gynecology September 25-29 at the Lewis Memorial Maternity Hospital. This year's program is made possible through the cooperation of E. R. Squibb & Sons and the Radio Corporation of America. There will be large television screens located throughout the hospital, so that it will be possible for small groups to gather before each screen and see details of the operative technic. There will also be discussions of pertinent topics carried on by the faculty of the department of obstetrics and gynecology and the guest speakers. Among the guests who will participate are Drs. William J. Dieckmann, chairman, department of obstetrics and gynecology, University of Chicago; Ralph A. Reis, professor and Ronald R. Greene, associate professor of obstetrics and gynecology, Northwestern University; Harry A. Oberheiman, chairman, department of surgery, Stritch School of Medicine, and John J. Madden, professor and chairman of the department of neurology and psychiatry, Stritch School of Medicine.

INDIANA

Lecture on Treating Atomic Bomb Casualties.—Dr. Andrew C. Ivy of Chicago, vice president of the University of Chicago and chairman of Chicago's Civil Defense Committee, will outline plans for treating casualties in an atomic bombing, at the Tenth District Medical Society meeting in Whiting September 12. All Indiana county medical societies have been invited to send representatives to the meeting.

State Medical Meeting.—The annual session of the Indiana State Medical Association will be held September 25-27 with headquarters at French Lick Springs Hotel, under the presidency of Dr. Claude S. Black, Warren. Out of state speakers include:

Edgar S. Gordon, Madison, Wis., Newer Developments in Arthritis Therapy.
David A. Boyd Jr., Rochester, Minn., Psychologic Language of the Organs.
Hayes Martin, New York, Diagnostic Significance of a "Lump in the Neck."
Ralph M. S. Barrett, St. Louis, Anesthesiology—Its Economics.
Francis E. Senear, Chicago, Brayton Foundation speaker, Eczema of the Hand.
Owen H. Wangensteen, Minneapolis, Minn., Intestinal Obstruction.
S. Leon Israel, Philadelphia, Modern Treatment of Sterility.

There will be a panel discussion on "Total Hysterectomy vs. Subtotal Hysterectomy in Benign Lesions of the Fundus" Tuesday afternoon, with Dr. David A. Bickel, South Bend, as moderator, and another panel Wednesday morning on "Uses and Abuses of Antibiotics and Antihistamines," with Dr. Paul J. Fouts, Indianapolis, serving as moderator. At the annual banquet Wednesday at 6:30 p. m. the speakers will be Dr. Elmer L. Henderson, Louisville, Ky., President, American Medical Association, and Mr. Henry P. Throckmorton, Boston. Scientific and technical exhibits will be shown. The Woman's Auxiliary will meet in conjunction with the association.

KENTUCKY

Health Units Employ Medical Students.—During the summer months third and fourth year students in the University of Louisville School of Medicine were employed in some of the county health units in the state. This plan, inaugurated last summer, was found to help both the units and the students.

Convalescent Hospital for Crippled Children.—A 48 bed Convalescent Hospital for the Kentucky Society for Crippled Children, on the Versailles Pike near Lexington, was opened August 1. This hospital, located on a 10 acre tract of ground purchased in 1943, is the result of several years of planning and work by county chairman, board members, volunteer workers, staff members and other interested persons.

LOUISIANA

Fellowships in Cardiology.—The Louisiana Heart Association announces two one-year fellowships in cardiology, to be known as the Charles Payne Fenner Jr. Memorial Fellowship and the Leon H. Rittenberg Fellowship, amounting, respectively, to $2,400 and $3.000 each. These will be opened to doctors having previously served at least one year of internship and one or more years of formal resident training in internal medicine or pediatrics. The purpose is to further research and provide additional clinical training in cardiovascular disease. Applications should be mailed to Dr. Allan M. Goldman, Secretary-Treasurer, Louisiana Heart Association, 3439 Prytania Street, New Orleans.

MARYLAND

Development Project to Aid Johns Hopkins Institutions.—A redevelopment project has been approved for the immediate vicinity of the Johns Hopkins Medical Institutions in East Baltimore. The project will cover a nine block area facing on the west side of Broadway, directly opposite the main entrance to the hospital. Its completion will see overcrowded, dilapidated and unsanitary structures replaced by modern garden apartments, stores, student dormitories, a hotel and an office building for physicians. It will solve a problem of providing suitable housing in the vicinity of the institution for students, staff members and their families, patients and visitors. The first step toward solution, not only of the Johns Hopkins problem but of other blighted areas in the city, was taken several years ago by special act of the Maryland State Legislature, which authorized the establishment of the Baltimore Redevelopment Commission to promote the interest of private builders and investors in rebuilding deteriorated areas. The Redevelopment Commission's function is to acquire the property through bargaining or condemnation proceedings, clear the land and make available such sites through sale or lease to private contractors who agree to undertake improvements in accordance with approved plans. The project will be financed by a $5,000,000 city bond issue, approved by the voters in 1948, and a two-to-one matching by federal funds which were made available for redevelopment purposes under the Housing Act of 1949. The Hopkins plans are moving ahead rapidly under the direction of the Medical Planning and Development Committee, consisting of the vice president of the university and hospital as chairman, the dean of the medical faculty, the director of the school of hygiene and public health and the director of the hospital. The recent final approval of the redevelopment project by the unanimous vote of the Baltimore City Council has removed a major obstacle from the future path of the medical institutions.

MICHIGAN

State Medical Meeting.—The annual session and postgraduate conference of the Michigan State Medical Society will be held September 20-22 at the Book-Cadillac Hotel, Detroit, under the presidency of Dr. William E. Barstow, St. Louis. Guest speakers will be:

Raymond W. McNealy, Chicago, Parotid Gland Tumors and Their Surgical Management.
Charles A. Doan, Columbus, Ohio, The Leukemic States: Their Differentiation and Specific Management.
W. Edward Chamberlain, Philadelphia, Newer Developments in Atomic Medicine.
Earl W. Netherton, Cleveland, Common Geriatric Dermatosis.
Lee F. Hill, Des Moines, Iowa, Preventive Pediatrics—Behavior Aspects.
George C. Prather, Brookline, Mass., Effect of Pregnancy on the Urinary Tract.
Samuel A. Cosgrove, Jersey City, N. J., Overcoming Hemorrhagic Mortality.
Harold W. Brown, New York, Management of Strabismus in Children.
Harris B. Shumacker Jr., Indianapolis, Aneurysms and Arteriovenous Fistulas.
Herbert F. Traut, San Francisco, Ovarian Cystomas.
Paul M. Moore Jr., Cleveland, Lesions of the Mouth.
Charles F. McKhann, Cleveland, Cerebral Birth Injury in Retrospect.
Vlado A. Getting, Boston, The Doctor's Responsibility in Atomic Diseases.
Antonio Rottino, New York, Hodgkin's Disease Treatment and Factors Influencing Results.
William A. Altemeier, Cincinnati, Clinical Use of the Newer Antibiotics in Surgery.
William F. Mengert, Dallas, Texas, Does Uterine Myoma Always Mean Operation?
John L. McKelvey, Minneapolis, Problems of Midpelvic Dystocia.
James T. Priestley, Rochester, Minn., Surgical Lesions of the Stomach.
Frederick F. Yonkman, Summit, N. J., Clinical Application of Adrenergic Blockade in Sympathetic Predominance.
Louis A. Brunsting, Rochester, Minn., Present Status of the Syphilis Problem.
Priscilla White, Boston, NPH-50 Insulin.
Frederick A. Gibbs, Chicago, Modern Treatment of Epilepsy.
William F. Rienhoff Jr., Baltimore, Carcinoma of the Lung.
William L. Bradford, Rochester, N. Y., Diagnosis, Treatment and Prevention of Whooping Cough.
John R. McDonald, Rochester, Minn., Clinical Importance of "Early Cancer."
Warren H. Cole, Chicago, Obstruction of the Common Duct by Stone.
Edward L. Bortz, Philadelphia, The Elderly Patient.

A general public meeting will be held Wednesday evening. The program includes the Biddle Lecture by John O. Christianson, Sc.D., St. Paul, on "Rediscovering America." Section meetings will be held each afternoon, and discussion conferences are scheduled each day from 5:00 to 6:00 p. m.

MINNESOTA

Dr. Adams to Head New Pediatrics Department.—Dr. John M. Adams, associate professor of pediatrics at the University of Minnesota Medical School, Minneapolis, has been named chairman of the department of pediatrics at the new medical school now being organized at the University of California at Los Angeles. Classes will not begin until 1952, but Dr. Adams will assume his duties this fall. He is a graduate of Columbia University College of Physicians and Surgeons, New York (1933) and obtained his Ph.D. degree at the University of Minnesota in 1942. He has been on the full time staff at the university since 1943.

Colvin Surgical Fund.—The Colvin Memorial Surgical Fund to carry on a research and teaching program at Ancker Hospital, St. Paul, has been established in memory of Dr. Alexander R. Colvin, who died on March 22, 1948. Dr. Colvin was associated with Ancker Hospital for over 50 years and was chief of the surgical services at the hospital for more than 30 years. Dr. Wallace P. Ritchie is director of the fund. Contributions have thus far been made by doctors who practice at the hospital. Other contributions should be made payable to the Colvin Memorial Surgical Fund and sent to Dr. Thomas E. Broadie, Superintendent, Ancker Hospital, St. Paul.

MISSOURI

Study Club Program.—The following programs for 1950 have been arranged by the General Practitioners Study Club of Greater St. Louis. All speakers are from St. Louis.

Sept. 20, Roy V. Boedeker, Office Gynecology.
Oct. 19, Charles F. Sherwin, Type of Superficial Cancer Suitable for Treatment by the General Practitioner.
Nov. 15, Robert J. Mueller, Significance of Headache to the General Practitioner.
Dec. 20, Robert A. Woolsey, Low Back Pain.

County Health Forum Lectures.—The program of the Jackson County Health forum lecture series for 1950-1951, sponsored by the auxiliaries of the accredited hospitals of Jackson County, is as follows:

Sept. 20, James H. Black, Dallas, Texas, Modern Progress in Allergy.
Oct. 18, Arnold S. Jackson, Madison, Wis., Use and Abuse of Cathartics.
Nov. 15, Henry H. Turner, Oklahoma City, Your Glands and the Aging Process.
Jan. 17, Wallace E. Herrell, Rochester, Minn., Bacterial and Virus Diseases and Antihistamine.
Feb. 21, E. Alton Ochsner, New Orleans, Cause and Prevention of Blood Clots.
Mar. 21, Morris Fishbein, Chicago, Prolongation of Life and Health.
Apr. 18, Charles Cameron, New York, Progress in Cancer Research.

All lectures are held promptly at 8:15 p. m. at the Little Theatre of the Municipal Auditorium, Kansas City, on the third Wednesday night of each month. These lectures are free and open to the public.

Annual Clinical Conference at Kansas City.—The annual fall Clinical Conference of the Kansas City Southwest Clinical Society will be held at the Municipal Auditorium in Kansas City October 2-5. Guest speakers include:

Joseph S. Barr, Boston, Bursitis: Acute, Subacute and Chronic.
Brian B. Blades, Washington, D. C., Pulmonary Lesions Amenable to Surgery.
Edward W. Boland, Los Angeles, Relation of the Adrenal Cortex to Rheumatic Disease.
William L. Bradford, Rochester, N. Y., Infection of the Newborn.
Edwin N. Broyles, Baltimore, Clinical Significance of Hoarseness.
Paul R. Cannon, Chicago, Some Recent Advances in Parenteral Alimentation.
F. Bayard Carter, Durham, N. C., Differential Diagnosis of Chronic Pelvic Pain.
Arthur Grollman, Dallas, Texas, Acute Anuria: Pathogenesis and Treatment.
Elmer Hess, Erie, Pa., Urologic Hints for the General Practitioner.
Charles L. Martin, Dallas, Texas, Roentgen Diagnosis of Peptic Ulcer.
E. Alton Ochsner, New Orleans, Venous Thrombosis.
Herman E. Pearse, Rochester, N. Y., Practical Considerations of Biliary Surgery.
Francis E. Senear, Chicago, Eczematoid Conditions of the Hands.
Dwight L. Wilbur, San Francisco, Management of Gastrointestinal Bleeding.
Irving S. Wright, New York, Modern Treatment of Coronary Thrombosis.
Mr. Clem Whitaker, Chicago, The Broadening Front Against State Socialism.
Miss Leone Baxter, Chicago, Medical Freedom and How to Keep It.

Other features of the program include a clinicopathologic conference Monday evening, round-table luncheons, sectional lecture groups and scientific and technical exhibits.

NEW YORK

Child Guidance Clinic Center.—A new traveling child guidance clinic for upstate New York areas was placed in operation by the State Department of Mental Hygiene on September 1. The clinic team, consisting of a psychiatrist, a psychologist and two psychiatric social service workers, is under the supervision of Dr. Anne M. Hart, who was formerly associated with Kings County Hospital, Brooklyn. Clinic headquarters will be located at Champlain College, Plattsburg, and the clinic will serve Plattsburg, Malone, Canton, Ogdensburg, Lake Placid, Tupper Lake, Elizabethtown and other nearby communities. The new center brings to 11 the total of traveling child guidance clinic teams operated by the department of mental hygiene.

Grants for Rheumatic Fever.—Westchester Heart Association has made a grant of $10,000 to Dr. Harold C. Anderson of Irvington House, Irving-on-Hudson, and his associate, Dr. Reginald A. Higgons, of St. Lukes Convalescent Hospital, Port Chester, for the purpose of making cortisone available free of charge to Westchester residents suffering from acute rheumatic fever. If the patient can afford hospital expenses he will be expected to pay them; otherwise arrangements will be made. The case must be referred early and must not have received prior antirheumatic therapy; the patient must agree to be admitted to Irvington House (ages 6-14) or Grasslands, Valhalla, (ages 14 and over) or to St. Lukes Convalescent Hospital (any age) and to be treated by staff physicians. No charge for professional care will be made by these physicians. Cases will be admitted only on the recommendation of the patient's private physician or any hospital clinic, provided specified manifestations of rheumatic fever are present.

New York City

Personal.—Dr. Alexander Brunschwig, chief, gynecologic service, Memorial Center for Cancer and Allied Diseases, has been awarded a medal from the University of Brussels in recognition of his services to medicine and humanity. While in Belgium this summer Dr. Brunschwig gave a series of lectures and surgical demonstrations at the meetings of La Journee Medical Bruxelloise and also addressed the staff of the Jules Bordet Institute of Brussels.

Course in Orthopedic Surgery.—Postgraduate training in orthopedic surgery will be given at the Hospital for Joint Diseases this fall. The course, being offered in affiliation with Columbia University College of Physicians and Surgeons, will consist of 11 morning and 11 afternoon sessions held on consecutive Thursdays beginning September 28 and ending December 14. The curriculums will include lectures, case demonstrations, conferences on the clinical, diagnostic, therapeutic, pathologic, bacteriologic and chemical aspects of skeletal disease, integrated to present a review of the modern concept of the more important orthopedic diseases. There will be opportunity for clinical examination of patients. Applications for registration should be made to the office of the Assistant Dean, Graduate Medicine, Columbia University College of Physicians and Surgeons, 630 West 168th Street, New York 23.

City Hospital Board.—Ten prominent physicians and laymen have been appointed by Mayor O'Dwyer as unsalaried members of the newly created Board of Hospitals, policy-making agency for the Department of Hospitals. Physician members, whose terms end on June 30 of the designated year, are Drs. Edward M. Bernecker, administrator of hospital service for the New York University-Bellevue Medical Center (1955); Thomas M. Rivers, physician in chief of the Rockefeller Institute for Medical Research (1954); Willard C. Rappleye, dean Columbia University College of Physicians and Surgeons (1953); Stanhope Bayne-Jones, president of the joint administrative board of the New York Hospital and Cornell Medical Center (1952), and George Baehr, president and medical director of the Health Insurance Plan of Greater New York (1951). Laymen members are David M. Heyman, president of the New York Foundation (1955); John A. Coleman, a governor of the New York Stock Exchange (1954); Mrs. Albert D. Lasker, secretary of the Albert and Mary Lasker Foundation (1953); Winthrop Rockefeller, chairman of the board of trustees of New York University-Bellevue Medical Center (1952), and Alfred P. Sloan Jr., chairman of the board of trustees of the Sloan Kettering Institute for Cancer Research. The Board of Hospitals was created by local law signed by the mayor on July 27. Its chairman is Dr. Marcus D. Kogel, commissioner of hospitals. Future appointments are to be for five years.

OHIO

Appointed to Research Council.—Dr. William A. Altemeier, of the University of Cincinnati College of Medicine faculty, has been appointed as a member of the National Research Council, Washington, D. C., for a term of three years. Dr. Altemeier is assistant professor of surgery in the college of medicine, from which he was graduated in 1934.

Faculty Appointments.—Four physicians have been appointed to the Western Reserve University School of Medicine, Cleveland. Dr. William E. Abbott, Detroit, has been appointed associate professor of surgery. He is a 1937 graduate of the school of medicine, was a Lee McBride Fellow in Surgery at the university and worked as a demonstrator in surgery at the university. In 1943 he went to Wayne University College of Medicine, Detroit, as an instructor in surgery; he was promoted to assistant professor of surgery in 1944, remaining until 1946.

Dr. T. George Bidder, Cleveland, newly appointed assistant professor of pharmacology, was a teaching fellow at Western Reserve University in 1946-1948. He received his medical degree from the university in 1942. The other pharmacologist joining the staff as associate professor of pharmacology is Dr. Giulio L. Cantoni, a graduate of the University of Milan in 1939. Dr. Roger B. Scott, Baltimore, joins the faculty as associate professor of obstetrics and gynecology. He received his medical degree from Johns Hopkins in 1938 and has been associated with Johns Hopkins Hospital since he interned there in 1938-1940.

TEXAS

School for Cerebral Palsied.—Plans for the Moody State School of Cerebral Palsied Children, Galveston, have been announced recently. The school, which is to be an affiliate of the University of Texas Medical Branch, will have a capacity of about 36 children and will be a treatment center for intensive therapy and education. It is ready to receive doctors' recommendations for candidates. Children who are acceptable must be between five and 12 years old, must be educable and treatable and must have some definite facility for follow-up treatment on release from the school. Routine care will be given at the school; however, children whose conditions are complicated by other diseases or severe nutritional problems will not be accepted. Further information concerning the program and application forms may be obtained from Miss Robertine St. James, R. P. T., Director, Box S, Capitol Station, Austin.

UTAH

Dr. Karr to Direct Radiation Therapy.—Dr. John W. Karr, an instructor in radiology at the University of Rochester (N. Y.) School of Medicine and Dentistry, has resigned to accept a post as director of radiation therapy at the University of Utah School of Medicine, Salt Lake City. Dr. Karr will organize a program for the use of radioactive isotopes in therapy at Salt Lake General Hospital, in addition to taking charge of all roentgen therapy work. He will serve also as associate coordinator of cancer teaching at the medical school. Dr. Karr received his medical degree from the University of Rochester in 1936. He joined the faculty on a part time basis in 1939 as instructor in pathology and radiology and became a full time instructor in 1946.

WEST VIRGINIA

State Grievance Committee.—The West Virginia State Medical Association at its last meeting approved the formation of a grievance committee, composed of five past presidents of the association, empowered to hear complaints against members of the association which may be made by laymen. The committee may elect its own chairman and adopt such policies, rules and regulations as may be agreed on by a majority of the members. If the committee cannot adjudicate the differences between the persons concerned, its findings are reported in writing to the component society of which the doctor complained against may be a member.

Tuberculosis and Health Association Meeting.—Dr. Edward T. Blomquist, assistant medical director of the Division of Tuberculosis, U. S. Public Health Service, Washington, D. C., and Mr. James G. Stone of the National Tuberculosis Association, New York City, will be guest speakers at the annual meeting of the West Virginia Tuberculosis and Health Association at the West Virginian Hotel in Bluefield September 20-21. A breakfast x-ray symposium featuring unusual chest conditions has been arranged for Thursday morning. Dr. E. Lyle Gage of Bluefield will preside, and Dr. Virgil L. Kelly of the Bluefield Sanitarium will lead the discussion. Assisting will be Dr. Hugh S. Edwards, Beckley, superintendent of Pinecrest Sanitarium; Dr. Archie L. Starkey, superintendent of Hopemont Sanitarium, and Dr. James H. Nelson Jr., superintendent

of Denmar Sanatorium. Mr. E. P. Wells, executive secretary of the Maine Tuberculosis Association and former executive secretary of the West Virginia Tuberculosis and Health Association, will be the guest speaker at the banquet.

WYOMING

State Medical Meeting.—The annual meeting of the Wyoming State Medical Society will be held in Cody September 7-9, under the presidency of Dr. DeWitt Dominick of Cody. Out of state speakers are as follows:

Warfield M. Firor, Baltimore, Breast Tumors.
Clement A. Finch, Seattle, Present Status of Treatment of Leukemia.
Norman F. Miller, Ann Arbor, Mich., Control of Cancer of the Cervix.
George F. Lull, Secretary and General Manager, American Medical Association, Chicago, National Legislation Affecting Medical Associations.
Fred H. Allen Jr., Boston, Some Problems Related to the Blood Groups of Mankind.
Howard P. Rome, Rochester, Minn., Problem of Sedatives and Narcotics.
Robert R. Kierland, Rochester, Minn., Cutaneous Manifestations of Systemic Disease.

ALASKA

Territorial Medical Association Meeting.—The annual convention of the Alaska Territorial Medical Association was held in McKinley Park, Alaska, August 17-19. Guest speakers included:

Donald V. Trueblood, Seattle, Breast Complications.
John R. Hand, Portland, Ore., Kidney Disease of Surgical Significance.
Thomas B. Carlile Jr., Seattle, Technic and Interpretation of Pyelograms.
Carl D. F. Jensen, Seattle, Treatment of Ocular Injury.
Mr. A. W. Murray, Seattle, Legal Aspects of Malpractice.

GENERAL

Essay Award on Chest Diseases.—The American College of Chest Physicians offers a cash prize award of $250 for the best original contribution, preferably by a young investigator, on any phase of chest disease. The prize is open to contestants of other countries as well as those of the United States. The winner will be announced at the meeting of the college in Atlantic City, N. J., June 7-10, 1951. The following conditions must be observed. Five copies of the manuscript, typewritten in English, should be submitted to the Executive Office of the college, 500 North Dearborn Street, Chicago 10, not later than April 1, 1951. The only means of identification of the author or authors shall be a motto or other device on the title page, and a sealed envelope bearing the same motto or device on the outside enclosing the name of the author or authors.

Employ the Physically Handicapped Week.—October 1-7 has been set as the sixth annual National Employ the Physically Handicapped Week, authorized by the Seventy-Ninth Congress in 1945. There are an estimated seven million physically handicapped persons in the nation's working population and another estimated one million unemployed, who can be added to the national working force if they were well informed and trained. Surveys conducted by the Department of Labor and the Veterans Administration, the Civil Service Commission, the U. S. Chamber of Commerce, the National Association of Manufacturers and the Accident Prevention Department of the Association of Casualty and Surety Companies have produced overwhelming evidence that, when properly placed, the handicapped worker's performance is as good as or better than that of the unimpaired worker.

Annual Meeting of Blood Banks.—The third annual meeting of the American Association of Blood Banks will be at the Stevens Hotel, Chicago, October 12-14 under the presidency of Dr. Thomas H. Seldon, Rochester, Minn. Among the speakers will be Drs. Sidney O. Levinson, Chicago; James J. Griffitts, Bethesda, Md.; Alexander S. Wiener, Brooklyn, N. Y.; Capt. Lloyd R. Newhouser, M. C., U. S. N., Washington, D. C., and Ernest E. Muirhead, Dallas, Texas. Panel discussions at the luncheon tables on Thursday and Friday will be held from noon until 2 p. m. The subjects will be Whole Blood Cell Suspension and Plasma Transfusions, Plasma Irradiation, Blood Derivatives and Plasma Substitutes, Administrative Problems in Blood Banks, Blood Grouping and Crossmatching, Rh Testing and Antibody Titration, Transfusion of Infants, Transfusion Reactions and Standards of Blood Banking.

Fatal Home Accidents Decline.—Home accidents currently claim about 30,000 lives yearly in the United States, according to the statisticians of the Metropolitan Life Insurance Company. Nonfatal home accidents resulting in more or less serious injury total about 4,500,000 annually. Nevertheless, progress during the past 15 years in reducing the frequency of fatal home accidents is reported. During this time, among the company's industrial policyholders the death rate from this cause has fallen from 13.6 to 8.1 per 100,000, a drop of 40 per cent. The decrease in mortality has been more pronounced for adults than for children, and somewhat greater for women than for men. An important contributing factor in bringing about the decrease has been the modernization of the American home, making it a safer place to live. The death rate from burns and scalds among girls and women is now less than half of what it was only 15 years ago.

Neurosurgical Society Meeting. — The Neurosurgical Society of America will hold its third annual meeting September 14-16 at the Cloisters, Sea Island, Ga. A clinicopathologic conference will be presented Thursday morning and papers in the afternoon. A panel will be held Friday morning on "Herniated Lumbar Intervertebral Disks," with Dr. Everett F. Hurteau, Akron, Ohio, as moderator. The discussants will be Drs. George J. Ehni, Houston, Texas; William A. Nosik, Cleveland; Rex H. Wilson, Akron, Ohio; Ernest H. Wood Jr., New York, and George S. Phalen, Cleveland. Another panel discussion will be presented Saturday morning on "Hydrocephalus," with Dr. George E. Roulhac, Washington University, St. Louis, as moderator. The discussants will be Drs. Claude M. Bertrand, Montreal, Canada; Donald D. Matson, Boston; Ira J. Jackson, Galveston, Texas, and Julius Wolkin, Cleveland. The annual dinner will be held Friday evening at 7:30 p. m.

Prevalence of Poliomyelitis.—Reports of cases of poliomyelitis for the periods indicated have been received from the National Office of Vital Statistics, U. S. Public Health Service.

	Week Ended		Total*		5-Year
	Aug. 19, 1950	Aug. 20, 1949	1950	1949	Median, 1945-1949
United States Total	1,480	3,416	9,097	16,375	8,374
New England States:					
Maine	3	40	21	180	10
New Hampshire	..	15	3	57	11
Vermont	2	16	8	30	9
Massachusetts	17	180	81	543	62
Rhode Island	2	14	11	35	10
Connecticut	12	89	84	162	45
Middle Atlantic States:					
New York	191	601	775	1,982	377
New Jersey	42	129	205	408	208
Pennsylvania	69	69	251	194	173
East North Central States:					
Ohio	83	209	261	592	213
Indiana	29	70	99	556	82
Illinois	104	348	433	1,230	280
Michigan	83	325	333	994	162
Wisconsin	21	78	126	339	129
West North Central States:					
Minnesota	22	136	113	689	270
Iowa	46	114	353	474	202
Missouri	32	106	123	600	85
North Dakota	5	32	16	235	31
South Dakota	11	25	39	110	68
Nebraska	20	41	146	192	183
Kansas	18	55	129	336	89
South Atlantic States:					
Delaware	3	7	12	23	23
Maryland	27	10	86	49	25
District of Columbia	10	9	75	33	33
Virginia	68	21	481	119	119
West Virginia	17	29	113	178	29
North Carolina	30	14	255	111	49
South Carolina	21	2	238	42	42
Georgia	19	5	115	86	69
Florida	19	11	133	114	114
East South Central States:					
Kentucky	42	42	257	252	54
Tennessee	36	41	217	296	157
Alabama	27	6	156	121	96
Mississippi	15	18	171	184	68
West South Central States:					
Arkansas	17	54	142	632	77
Louisiana	17	6	178	123	69
Oklahoma	25	71	270	732	189
Texas	113	104	1,515	1,446	602
Mountain States:					
Montana	1	2	11	22	15
Idaho	2	33	26	223	46
Wyoming	4	14	25	52	45
Colorado	13	60	65	218	58
New Mexico	2	7	36	77	36
Arizona	1	20	45	71	48
Utah	4	11	17	63	30
Nevada	..	...	1	10	3
Pacific States:					
Washington	25	29	102	165	79
Oregon	29	7	166	66	39
California	63	115	653	839	591

* Beginning with 12th week of each year.

LATIN AMERICA

WHO to Aid in Eradication Campaigns.—In response to a request of the Government of Mexico for the development of an intensive vaccination campaign against smallpox in that country, the Pan American Sanitary Bureau has sent Dr. Abraham B. Horwitz to Mexico City. Dr. Horwitz, who recently joined the staff of the bureau, is a graduate of the University of Chile at Santiago. He received his master's degree in public health at Johns Hopkins University, Baltimore, and has for several years been professor of contagious diseases at the School of Medicine of the University of Chile and the School of Public Health in Santiago.

Aid in a campaign undertaken by several South American governments against hydatidosis will be given by the Pan American Sanitary Bureau. The affected area is in the great livestock country of the Pampas, with its greatest focus in southern Brazil, Uruguay and northern Argentina. The chief of its Veterinary Public Health Section, Benjamin D. Blood, D.V.M., Washington, D. C., will visit these countries to study field problems and methods of control.

FOREIGN

Personal.—Dr. Paul Werner, chief of the gynecologic department of the Krankenhaus der Stadt, Vienna, Austria, has begun a five month visit to South America as guest of the universities of Brazil, Argentina, Uruguay and Chile, where he will conduct postgraduate courses.

Medical Mission to Germany.—The Unitarian Service Committee has organized, in cooperation with the U. S. Department of State, a second medical mission to Germany to exchange information, to make personal contacts, to study the conditions of German universities, to ascertain their needs and to observe their reconstruction. Members of the mission are participating in ward rounds, seminars and laboratory demonstrations. Members of the mission are Drs. Erwin W. Straus, Lexington, Ky., chairman; Alfred E. Farah, Syracuse, New York; Halvor N. Christensen, Ph.D., Boston; John B. Dillon, Los Angeles; Thomas R. Forbes, Ph.D., New Haven, Conn.; William P. Longmire Jr., Los Angeles; Richard H. Lyons, Syracuse, N. Y.; Eric Ogden, Columbus, Ohio; Francis F. Schwentker, Baltimore, and J. Robert Wilson, Philadelphia.

Tuberculosis Control Centers in India.—Three tuberculosis control demonstration centers in India are to be set up by the government with the assistance of the World Health Organization and the United Nations International Children's Emergency Fund. The centers will be at Delhi, Patna and Trivandrum. The objective is to introduce into India modern methods of tuberculosis control and to train local medical and public health personnel in these methods. An estimated half million persons die each year in India from tuberculosis. Each center will provide a dispensary service with x-ray and laboratory equipment. A team of four or five WHO medical and technical workers will operate each center for at least a year. The Indian Health Ministry has granted an equivalent of $45,000 to the Tuberculosis Association of India for construction of a center in Delhi and the equivalent of $26,000 for the Bihar government center at Patna. UNCEF will provide supplies and equipment as well as a number of fellowships for study.

Health Aid for Indo-China.—The public health phase of the United States economic program for Indo-China is reported scheduled to begin in August. About $6,000,000 of the $23,500,000 allotted for economic aid will be devoted to public health projects. In addition, the United Nations International Children's Emergency Fund and the World Health Organization are expected to spend more than $300,000 on coordinated projects. In the northern part of the country malaria has become widespread. Trachoma, venereal disease, tuberculosis and yaws are widely prevalent. Warfare has destroyed 13 of the 19 professional hospitals in northern and central Vietnam. Four prefabricated hospitals of mobile hospital units are to be brought in. A training program is included. The need for medical personnel is shown by the fact that in a population of 17,500,000 there are only 390 doctors, or one for nearly 12,000 persons. In Cambodia the ratio is one doctor for every 71,000 and in Laos one to every 100,000.

Philippines Needs Packages and Books.—There are an estimated 300,000 cases of tuberculosis in the Philippines, yet there are only 1,500 hospital beds for victims, 1,000 of them at Quezon Institute, on the outskirts of Manila, according to Dr. Fernando B. Duran, a member of the sanitarium's staff. The sanitarium also provides clinic care for 300 ambulatory cases. But lack of the most basic supplies, food, clothing, linens and up-to-date books on medicine's methods of attacking the disease combine to hinder the institution's program. During World War II bombs battered the institute, destroying some of its 10 buildings and damaging others. The hospital's medical library was totally demolished. The supplies needed to fight tuberculosis can be sent by Americans through CARE, 20 Broad Street, New York, or any local CARE office. Ten dollars will provide a CARE package of food or a household linen package containing the sheets, pillowcases and towels that are a necessary part of hospital supplies. Five-fifty dollars will send a cotton textile package to provide dresses and suits for patients. A contribution to the CARE-UNESCO Book Fund will send the latest American books on tuberculosis to bring the institute's staff up to date on medical technics.

CORRECTION

International Medical Women's Meeting.—Dr. Ada Chree Reid of New York City is a candidate for the office of president of the Medical Women's International Association, holding its congress in Philadelphia September 10-16, and not president-elect as was stated in THE JOURNAL August 12, page 1354.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Chicago, Oct. 8-11. Sec., Dr. Curtiss B. Hickcox, 745 Fifth Ave., New York 22.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written.* Various locations, Sept. 14. *Oral.* Detroit, Oct. 20-22. Sec., Dr. George M. Lewis, 66 East 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 16. Asst. Sec., Dr. William A. Werrell, 1 West Main Street, Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Chicago, Oct. 20-21, 1950. Applications no longer accepted. Sec., Dr. W. J. German, 789 Howard Ave., New Haven, Conn.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral, including sub-specialties,* Oct. 26-28. Final date for filing application was August 19. *Oral, including sub-specialties,* Dec. 7-9. Executive Secretary-Treasurer, Dr. William A. Werrell, 1 West Main St., Madison 3.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, Jan. 5-6, 1951. *Oral.* Chicago, Oct. 2-6; San Francisco, March 11-15; New York, May 31-June 4; Chicago, October 1951. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago, Jan. 25-26. Final date for filing applications is Aug. 15, 1950. Sec., Dr. Harold A. Sofield, 122 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 3-6, Jan. 8-11, 1951. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PATHOLOGY: St. Louis, Oct. 13-14. Sec., Dr. Robert R. Moore, 507 Euclid Ave., St. Louis 10.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 13-15 and Boston, Dec. 1-3. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: Houston, Nov. 30, Dec. 1-2. Sec., Dr. Bradford Cannon, 4647 Pershing Ave., St. Louis.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH: St. Louis, Oct. 28-29. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY: Philadelphia, Nov. 11-12, Part II—Anorectal Surgery. Sec.-Gen., Dr. Louis A. Buie, 102-110 Second Ave., S.W., Rochester.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 18-19. Final date for filing applications is Sept. 1. Sec., Dr. Francis J. Braceland, 102-110 Second Ave., S.W., Rochester.

AMERICAN BOARD OF RADIOLOGY: Chicago, Dec. 5-10. Quota of appointments already filled. Sec., Dr. B. R. Kirklin, Mayo Clinic, Rochester.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, Oct. 25. *Written.* Various centers, March 1951. Final date for filing applications is Dec. 1, 1950. Sec., Dr. J. Stewart Rodman, 225 South 15th Street, Philadelphia.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 10-14, 1951. Final date for filing applications is Sept. 1, 1950. Sec., Dr. Harry Culver, 7935 Sunnyside Road, Minneapolis 21.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 26-28. Sec., Dr. D. G. Gill, 519 Dexter Ave., Montgomery.

ALASKA: * Juneau, Sept. 5. Special examinations given on application. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARKANSAS: * Little Rock, Nov. 9-10. Sec., Dr. Joe Verser, Harrisburg. Homeopathic: Nov. Sec., Dr. C. S. Bungart, 105 N. 14th St., Ft. Smith. Eclectic: Nov. 9. Sec., Dr. C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Examination Written.* Sacramento, Oct. 16-19. *Examination, Oral and Clinical for Foreign Medical School Graduates,* San Francisco, Nov. 12. *Reciprocity, Oral Examination,* San Francisco, Nov. 11. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

COLORADO: * Denver, Jan. 3-5, 1951. Exec. Sec., Mrs. B. M. Hudgens, 831 Republic Bldg., Denver.

CONNECTICUT: * Hartford, Nov. 14-15. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven. Homeopathic: Nov. 14-15. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

DELAWARE: Dover, Jan. 9-11. *Reciprocity.* Jan. 18, 1951. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: * Washington, Sept. 18. Sec., Dr. Daniel L. Seckinger, 4130 Municipal Bldg., Washington.
FLORIDA: * Jacksonville, Nov. 26-28. Sec., Dr. Homer Pearson, 701 Dupont Bldg., Miami.
GEORGIA: Atlanta, Oct. 10-11. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.
HAWAII: Honolulu, Jan. 8-11, 1951. Sec., Dr. I. L. Tilden, 881 S. Hotel St., Honolulu.
IDAHO: Boise, Jan. 8, 1951. Sec., Mr. Armand L. Bird, 305 Sun Bldg., Boise.
ILLINOIS: Chicago, Oct. 10-12. Superintendent of Registration, Mr. Charles F. Kervin, Capitol Bldg., Springfield.
INDIANA: Indianapolis, June 1951. Exec. Sec., Miss Ruth V. Kirk, 1138 K. of P. Bldg., Indianapolis 4.
IOWA: *Written.* Des Moines, Dec. 4-6. Acting Director, Division of Examination and Licensure, State Department of Health, 1027 Des Moines St., Des Moines.
KANSAS: Topeka, Dec. 13-14. Sec., Dr. O. W. Davidson, 772 New Brotherhood Bldg., Kansas City.
LOUISIANA: New Orleans, Dec. 8-10. Sec., Dr. R. B. Harrison, 1507 Hibernia Bank Bldg., New Orleans.
MAINE: Portland, Nov. 14-15. Sec., Dr. Adam P. Leighton, 192 State St., Portland.
MARYLAND: Baltimore, Dec. 12-15. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1.
MASSACHUSETTS: Boston, Jan. 23-26, 1951. Sec., Dr. Geo. R. Schadt, 37 State House, Boston.
MINNESOTA:* Minneapolis, Oct. 17-19. Sec., Dr. J. F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.
MISSISSIPPI: Jackson, December. Asst. Sect., Dr. R. N. Whitfield, Jackson 113.
MONTANA: Helena, Oct. 2. Sec., Dr. S. A. Cooney, 7 W. 6th Ave., Helena.
NEBRASKA:* June 1951. Director, Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln.
NEW HAMPSHIRE: Concord, Sept. 13. Sec., Dr. John Samuel Wheeler, 107 State House, Concord.
NEW JERSEY: Trenton, Oct. 17-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.
NEW MEXICO: * Santa Fe, Oct. 9-10. Sec., Dr. Charles J. McGoey, Coronado Building, Santa Fe.
NEW YORK: New York, Buffalo, Albany and Syracuse, Oct. 3-6. Sec., Dr. Jacob L. Lochner, 23 S. Pearl St., Albany.
NORTH CAROLINA: *Reciprocity.* Raleigh, Sept. 25. Sec., Dr. Ivan Procter, 226 Hillsboro St., Raleigh.
NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. C. J. Glaspel, Grafton.
OHIO: Columbus, December. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.
OREGON: * *Examination.* Portland, January 1951. *Reciprocity.* Portland, Oct. 13. Sec., Mr. Howard I. Bobbit, 608 Failing Bldg., Portland 4.
PENNSYLVANIA: Philadelphia, January 1951. Acting Secretary, Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.
PUERTO RICO: *Examination.* Santurce, Sept. 5-9. Sec., Mr. Luis Cueto, Coll, Box 3717, Santurce.
RHODE ISLAND: * Providence, Oct. 5-6. Chief, Mr. Thomas B. Casey, 355 State Office Bldg., Providence.
SOUTH CAROLINA: Columbia, Nov. 13-15. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.
TENNESSEE: * Memphis, Sept. 27-28. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.
TEXAS:* Fort Worth, November 9-11, 1950. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth.
UTAH: Salt Lake City, July 1951. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.
VERMONT: Burlington, February 1951. Sec., Dr. F. J. Lawliss, Richford.
VIRGINIA: Richmond, Nov. 30, Dec. 1-2. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.
WASHINGTON: * Seattle, January 1951. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.
WEST VIRGINIA: Charleston, Oct. 2-4. Sec., Dr. N. H. Dyer, State Capitol, Charleston 6.
WISCONSIN: * River Falls, Jan. 9-11, 1951. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.
WYOMING: Cheyenne, Oct. 2. Sec., Dr. Franklin D. Yoder, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* Juneau, last week in August. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.
ARIZONA: Tucson, Sept. 19. Sec., Mr. Francis A. Roy, Science Hall, Univ. of Arizona, Tucson.
ARKANSAS: Little Rock, Oct. 3-4. Sec., Mr. L. E. Gebauer, 1002 Donaghey Bldg., Little Rock.
COLORADO: *Examination.* Denver, Sept. 13-14. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 3.
CONNECTICUT: Oct. 14. Executive Sec., M. G. Reynolds, State Board of Healing Arts, 110 Whitney Ave., New Haven 10.
DISTRICT OF COLUMBIA: Washington, Oct. 23-24. Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.
FLORIDA: Jacksonville, Nov. 11. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.
IOWA: Des Moines, Oct. 10. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.
MICHIGAN: *Examination.* Ann Arbor, Oct. 13-14. Sec., Miss Eloise LeBeau, 101 North Walnut Street, Lansing 15.
MINNESOTA: Minneapolis, Oct. 3-4. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis 14.
NEBRASKA: *Examination.* Omaha, Oct. 3-4. Director, Mr. Oscar F. Humble, Room 1009, State Capitol Building, Lincoln 9.
NEW MEXICO: *Examination.* Santa Fe, Sept. 17. Sec., Mrs. Marguerite K. Cantrell, Box 1522, Santa Fe.
OKLAHOMA: *Examination.* Oklahoma City, Sept. 15. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.
OREGON: *Examination.* Portland, Sept. 9. Sec., Dr. C. D. Byrne, University of Oregon, Eugene.
RHODE ISLAND: *Examination.* Providence, Nov. 8. Chief, Division of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Building, Providence.
SOUTH DAKOTA: Vermillion, Dec. 1-2. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.
TENNESSEE: Memphis, Sept. 21-22. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis 3.
TEXAS: *Examination.* Austin, Oct. 13-14, April 1951. Sec., Brother Raphael Wilson, 306 Nalle Building, Austin.
WASHINGTON: Seattle, January 1951. Sec., Mr. Edward D. Dohm, Department of Licenses, Olympia.
WISCONSIN: *Examination.* Milwaukee, Dec. 2. Sec., Mr. W. H. Barber, Scott and Watson Sts., Ripon.

Coming Medical Meetings

American Academy of Ophthalmology and Otolaryngology, Palmer House, Chicago, Oct. 8-13. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Secretary.
American Academy of Pediatrics, Palmer House, Chicago, Oct. 16-19. Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill., Secretary.
American Association of Blood Banks, Stevens Hotel, Chicago, Oct. 12-14. Miss Marjorie Saunders, 3301 Junius, Dallas 1, Texas, Secretary.
American Association of Obstetricians, Gynecologists and Abdominal Surgeons, The Homestead, Hot Springs, Va., Sept. 7-9. Dr. Leroy A. Calkins, University of Kansas Medical Center, Kansas City 3, Secretary.
American Clinical and Climatological Association, Red Lion Inn, Stockbridge, Mass., Oct. 17-19. Dr. James Bordley III, Mary Imogene Bassett Hospital, Cooperstown, N. Y., Secretary.
American Hospital Association, Atlantic City, Sept. 18-22. Mr. George Bugbee, 18 E. Division St., Chicago 10, Executive Director.
American Society of Clinical Pathologists, Drake Hotel, Chicago, Oct. 17-21. Dr. Clyde G. Culbertson, 1040 W. Michigan St., Indianapolis 7, Secretary.
Biological Photographic Association, Hotel Sheraton, Chicago, Sept. 6-8. Mr. Lloyd E. Varden, Pavelle Color, Inc., 533 W. 57th St., New York City 19, Secretary.
Colorado State Medical Society, Broadmoor Hotel, Colorado Springs, Sept. 20-23. Mr. Harvey T. Sethman, 1612 Tremont Place, Denver 2, Executive Secretary.
Delaware, Medical Society of, Dover, Oct. 2-4. Dr. Andrew H. Gehret, 1007 Park Place, Wilmington, Secretary.
District of Columbia, Medical Society of the, Washington, Oct. 2-4. Mr. Theodore Wiprud, 1718 M Street N.W., Washington 6, Secretary.
Idaho State Medical Association, Sun Valley, Sept. 6-9. Dr. Alfred M. Popma, 220 N. First St., Boise, Secretary.
Indiana State Medical Association, French Lick, Sept. 25-27. Mr. Ray E. Smith, 23 E. Ohio St., Indianapolis 4, Executive Secretary.
Kentucky State Medical Association, Brown Hotel, Louisville, Sept. 26-28. Dr. Bruce Underwood, 620 S. Third St., Louisville 2, Secretary.
Michigan State Medical Society, Book-Cadillac Hotel, Detroit, Sept. 20-22. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing 8, Secretary.
Mississippi Valley Medical Society, Springfield, Ill., Sept. 27-29. Dr. Harold Swanberg, 510 Maine St., Quincy Ill., Secretary.
Nevada State Medical Association, Las Vegas, Oct. 5-7. Dr. Wesley W. Hall, 307 West Sixth St., Reno, Secretary.
New Hampshire Medical Society, Mt. Washington Hotel, Bretton Woods, Sept. 10-12. Dr. Deering G. Smith, 44 Chester St., Nashua, Secretary.
Oregon State Medical Society, Gearhart, Sept. 27-29. Dr. Werner E. Zeller, Medical-Dental Bldg., Portland 5, Secretary.
Pennsylvania, Medical Society of the State of, Philadelphia, Oct. 15-19. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh 22, Secretary.
Southwestern Surgical Congress, Shirley-Savoy Hotel, Denver, Colo., Sept. 25-27. Dr. C. R. Rountree, 525 N.W. Eleventh St., Oklahoma City, Secretary.
Vermont State Medical Society, Mt. Washington Hotel, Bretton Woods, N. H., Sept. 10-12. Dr. James P. Hammond, 128 Merchants Row, Rutland, Secretary.
Virginia, Medical Society of, Roanoke, Oct. 8-11. Mr. H. S. Johnson, 1200 East Clay St., Richmond 19, Executive Secretary.
Washington State Medical Association, Davenport Hotel, Spokane, Sept. 10-13. Dr. James W. Haviland, 338 White-Henry-Stuart Bldg., Seattle, Secretary.
Wisconsin, State Medical Society of, Hotel Schroeder and Milwaukee Auditorium, Milwaukee, Oct. 1-4. Mr. C. H. Crownhart, 704 E. Gorham St., Madison, Secretary.
Wyoming State Medical Society, Cody, Sept. 7-9. Dr. George H. Phelps, 1604 Capitol Ave., Cheyenne, Secretary.

International Meetings

International Congress on Cardiology, Paris, France, Sept. 3-9. Dr. Mouquin, 78 rue de l'Abbé-Groult, Paris 15e, France, Secretary-General.
International Congress on Criminology, Palais de la Sorbonne Grand Amphitheater, Paris, France, Sept. 10-19. M. Pierre Piprot d'Alleaume, 188 Ave. Victor Hugo, Paris 16e, France, General Secretary.
International Congress on Diseases of the Chest, Carlo Forlanini Institute, Rome, Italy, Sept. 17-22. Prof. A. Omodei Zorini, Carlo Forlanini Institute, Rome, Italy, Chairman.
International Congress of Experimental Cytology, New Haven, Conn., U. S. A., Sept. 4-8. Dr. Danielli, King's College, London, England, Secretary.
International Congress on Internal Medicine, Paris, France, Sept. 11-14. Prof. Justin Besancon, 38 rue Barbet de Jouy, Paris, France, Secretary.
International Congress of Psychiatry, Palais de la Sorbonne, Paris, France, Sept. 19-27. Dr. Henri Ey, 1 rue Cabanis, Paris 14e, France, General Secretary.
International Society for Internal Medicine, Paris, France, Sept. 11-15. Dr. Albert M. Snell, 102 Second Ave. S.W., Rochester, Minn., Chairman, American Committee.
International Union Against Tuberculosis, Copenhagen, Denmark, Sept. 1-8. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6e, France, Secretary.
Medical Women's International Association, Philadelphia, Penna., U. S. A., Sept. 10-16. Dr. Montreuil-Straus, 75 rue de l'Assomption, Paris, France, Secretary.
World Medical Association, Hotel Roosevelt, New York City, U. S. A., Oct. 16-20. Dr. Louis H. Bauer, 2 E. 103d St., New York City 29, Secretary-General.
World Federation for Mental Health, Cité Universitaire, Paris, France, Aug. 31-Sept. 7. Secretary, 19 Manchester St., London, W.1, England.

DEATHS

Bertner, Ernst William ● Houston, Texas; born in Colorado City, Texas, Aug. 18, 1889; University of Texas School of Medicine, Galveston, 1911; professor and chairman of the department of gynecology at Baylor University College of Medicine in the Texas Medical Center; in 1944 member of the House of Delegates of the American Medical Association; past president of the Texas State Medical Association, Harris County Medical Society, Post Graduate Medical Assembly of South Texas, Texas Surgical Society and the Texas Association of Obstetricians and Gynecologists; served as vice president of the Southern Medical Association, member of the executive committee of the Central Association of Obstetricians and Gynecologists and a fellow of the American College of Surgeons; member of the American Urological Association and Interurban Gynecological Society; was vice president of the American Cancer Society in 1949 and member of that society's board of directors for several years; was chairman of the executive committee of the Texas Division of the American Cancer Society and was awarded the society's distinguished service medal for cancer control work; executive committeeman of the Texas Social Hygiene Association; during World War I was assigned to the British Army Medical Corps, going overseas as a lieutenant in July 1917; transferred to the American forces in March 1918; discharged with the rank of major in June 1919; in command of the Emergency Medical Service of the Office of Civilian Defense for Harris County during World War II and received a Presidential Citation for this service; president and a founder of the Texas Medical Center; acting director of the M. D. Anderson Hospital for Cancer Research for the first four years of its existence, organized and directed that institution for the University of Texas until a full time director was named; served as chief of staff of Jefferson Davis Hospital and Hermann Hospital and on the surgical staffs of Memorial Hospital and Southern Pacific Hospital; initiated the annual cancer symposium at Anderson and this year established the Bertner Lectureship, which will bring to the symposium each year one who has done outstanding cancer research work; served as vice chairman of the Houston Board of Health; member of the board of directors of the Houston Chamber of Commerce and member of the national Citizens Committee for the Hoover Report; died July 28, aged 60, of carcinoma.

Woolsey, George ● New Haven, Conn.; born in New Haven May 2, 1861; College of Physicians and Surgeons, medical department of Columbia College, New York, 1885; emeritus professor of clinical surgery at Cornell University Medical College, New York; past president of the New York Surgical Society, New York Clinical Society and New York Gastroenterological Society; member of the Medical Society of the State of New York and the American Surgical Association; fellow of the American College of Surgeons; an Associate Fellow of the American Medical Association; consulting surgeon, Bellevue Hospital, Memorial Hospital, New York Infirmary for Women and Children in New York, Peekskill (N. Y.) Hospital and St. John's Riverside Hospital in Yonkers; author of "Applied Surgical Anatomy"; died July 1, aged 89, of pneumonia.

Hart, Vernon Lewis ● Minneapolis; born in Huron, Ohio, Oct. 24, 1898; University of Michigan Medical School, Ann Arbor, 1924; clinical assistant professor of orthopedic surgery at the University of Minnesota Medical School; formerly on the faculty of his alma mater; specialist certified by the American Board of Orthopaedic Surgery; member of the Clinical Orthopaedic Society and American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; in 1939 received the Southern Minnesota Medical Association's gold medal for the best scientific exhibit at the Minnesota State Medical Association; served during World War II; affiliated with Asbury, Abbott, St. Andrews, St. Barnabas, St. Mary's and Swedish hospitals; formerly associated with the Dayton Clinic in Dayton, Ohio; drowned in Cedar Lake July 12, aged 51.

Arrington, James Eland, Frederick, Okla.; University of Tennessee Medical Department, Nashville, 1905; member of the American Medical Association; past president of Tillman County Medical Society; served as city health officer; died June 11, aged 73, of cirrhosis of the liver.

● Indicates Fellow of the American Medical Association.

Baillie, William Finley ● Fargo, N. D.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1903; fellow of the International College of Surgeons; died in St. Luke's Hospital May 5, aged 72, of meningitis.

Beasley, John Johnson ● Pleasant Shade, Tenn.; University of Tennessee Medical Department, Nashville, 1904; died suddenly June 2, aged 74, of coronary thrombosis.

Bell, Felix Ortan, Burlington, N. C.; Emory University School of Medicine, Atlanta, 1918; member of the American Medical Association; served during World War I; died June 26, aged 61.

Brooks, Henry Wells ● Buena Vista, Ga.; Atlanta Medical College, 1916; died in St. Francis Hospital, Columbus, June 22, aged 55, of coronary occlusion.

Bryan, Henry Bohlen, Houston, Texas; George Washington University School of Medicine, Washington, D. C., 1905; died June 27, aged 88.

Carter, Albert Arthur ● Boston; Middlesex College of Medicine and Surgery, Cambridge, Mass., 1917; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the New England Ophthalmological Society; affiliated with Boston City Hospital, Massachusetts Eye and Ear Infirmary and Beth Israel Hospital; died in Malden June 23, aged 76.

Carter, Frank Henry, Melrose, Mass.; Medical School of Maine, Portland, 1882; died June 25, aged 92.

Caruthers, Veolo Oglesby, Colonial Beach, Va.; Medical College of Virginia, Richmond, 1909; died July 11, aged 65.

Caveny, Kasper Patrick, Portland, Ore.; University of Minnesota Medical School, Minneapolis, 1937; member of the American Medical Association; affiliated with Good Samaritan Hospital in Portland and Jones Hospital in Hillsboro; died in June, aged 43, of coronary insufficiency.

Compton, Arthur N., Valentine, Neb.; St. Louis College of Physicians and Surgeons, 1898; member of the American Medical Association; served as mayor, member of the city council and for many years on the board of education, of which he was chairman; died July 7, aged 77, of carcinoma.

Comstock, George Spaulding, Baldwin, N. Y.; University and Bellevue Hospital Medical College, New York, 1901; instructor in medicine at his alma mater from 1922 to 1925; veteran of the Spanish-American War and World War I; served as police surgeon in Rockville Centre; formerly on the staff of the Jamaica (N. Y.) Hospital and St. Anthony's Hospital in Woodhaven; died in U. S. Naval Hospital, St. Albans, June 24, aged 73.

Conn, Emmett Higbee, Los Angeles, Calif.; State University of Iowa College of Medicine, Iowa City, 1920; died June 27, aged 55.

Connamacher, Harold Solomon ● Newark, N. J.; Columbia University College of Physicians and Surgeons, New York, 1925; formerly a pharmacist; affiliated with Newark Beth Israel Hospital and Presbyterian Hospital; died July 9, aged 54, of coronary thrombosis.

Cornelius, Albert Franklin, Berea, Ky.; Hospital College of Medicine, Louisville, 1906; member of the American Medical Association; died in Pittsburgh June 6, aged 64.

Cottle, Louis Albert, Worcester, Mass.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; member of the American Medical Association; affiliated with Fairlawn Hospital; died June 21, aged 76, of cerebral hemorrhage.

Cross, Louis Kent, Winchendon, Mass.; Boston University School of Medicine, 1899; member of the American Medical Association; affiliated with Henry Heywood Memorial Hospital in Gardner; for many years trustee of the Winchendon Public library; died in Gardner July 5, aged 73, of arteriosclerotic heart disease.

Currer, Paul McAllister ● Milwaukee; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1910; past president and treasurer of the Milwaukee County Medical Society; affiliated with Evangelical Deaconess, Milwaukee County and Johnston Emergency hospitals; died July 8, aged 62, of heart disease.

Deans, Arthur Wood, Battleboro, N. C.; Medical College of Virginia, Richmond, 1915; member of the American Medical Association; member of the State Board of Conservation and Development; for many years mayor; affiliated with Park View Hospital in Rocky Mount; died July 1, aged 62, of coronary occlusion.

Eaves, James ✦ Oakland, Calif.; University of Edinburgh Faculty of Medicine, Scotland, 1910; member of the American Association of Industrial Physicians and Surgeons; past president of the American Medical Golfing Association; on the staff of St. Mary's Hospital in San Francisco and Providence Hospital; died July 3, aged 65, of heart disease.

Flickinger, George Harvey, Hopedale, Ill.; Chicago Medical School, 1934; member of the American Medical Association; president of the Tazewell County Medical Society; served during World War II; died July 10, aged 46, of cerebral hemorrhage.

Foxworth, Thomas Daniel, Pinewood, S. C.; University of the South Medical Department, Sewanee, Tenn., 1900; died in Holly Hill July 28, aged 78.

Frace, Guy Henry ✦ St. Johns, Mich.; Detroit College of Medicine, 1898; for many years city health officer; member and past chief of the staff of Clinton Memorial Hospital, where he died June 29, aged 76, of pneumonia.

Hartman, Eslie Helen ✦ Chicago; New York University College of Medicine, 1942; certified by the National Board of Medical Examiners; clinical instructor in medicine at the University of Illinois College of Medicine, where she was medical adviser for women in the health service; on the staff of the Illinois Masonic Hospital; killed July 13, aged 34, when an airplane fell into Lake Erie, near North East, Pa.

Hines, Herman Henry ✦ Pennington Gap, Va.; Medical College of Virginia, Richmond, 1935; also a graduate in pharmacy; served during World War II; died in St. Mary's Hospital, Norton, July 5, aged 42, of virus pneumonia.

Howard, William Arthur, Parkersburg, Iowa; Northwestern University Medical School, Chicago, 1905; died July 4, aged 73, when the automobile he was driving was struck by a train in Algona.

Hull, John Scudder ✦ Hicksville, Ohio; Eclectic Medical Institute, Cincinnati, 1896; vice president of the Hicksville Bank; died July 2, aged 77, of coronary occlusion.

Hummell, Harry Charles, Rochester, N. Y.; University of Buffalo School of Medicine, 1908; member of the American Medical Association; served as deputy city health officer; affiliated with St. Mary's, Highland and County hospitals; died July 5, aged 67, of cerebral hemorrhage.

Jesperson, Lydia ✦ Battle Creek, Mich.; University of Illinois College of Medicine, Chicago, 1913; formerly a medical missionary; for many years affiliated with Battle Creek Sanitarium; died in San Francisco July 11, aged 74, of myocardial infarction.

Jones, Samuel Alexander, Ramona, Okla.; Memphis (Tenn.) Hospital Medical College, 1903; died in Washington County Memorial Hospital, Bartlesville, July 4, aged 83.

Kasten, William Charles, Fort Madison, Iowa; Keokuk Medical College, College of Physicians and Surgeons, 1903; also a pharmacist; past president of Lee County Medical Society; affiliated with Sacred Heart Hospital; died July 7, aged 73, of cerebral hemorrhage.

Large, Wallace Bruce, Rochester, N. Y.; University of Toronto Faculty of Medicine, Toronto, Canada, 1907; served during World War I; died July 5, aged 73, of coronary thrombosis.

McGavock, Edward Pointer ✦ Wytheville, Va.; University of Virginia Department of Medicine, Charlottesville, 1893; emeritus professor of dermatology and syphilology at the Medical College of Virginia, Richmond; at one time associated with the Skin and Cancer Hospital in New York; died in Jefferson Hospital, Roanoke, July 3, aged 81, of myocardial failure and bronchial asthma.

Mays, Joseph W., St. Joseph, Mo.; Ensworth Medical College, St. Joseph, 1900; member of the American Medical Association; formerly county coroner; affiliated with St. Joseph's Hospital and Missouri Methodist Hospital; died July 10, aged 78, of hypostatic pneumonia and prostatic hypertrophy.

Meyer, Harry H., St. Louis; Missouri Medical College, St. Louis, 1897; member of the American Medical Association; died in St. John's Hospital July 22, aged 77, of pulmonary edema and carcinoma of the bladder.

O'Connor, Thomas Augustine, Topeka, Kan.; St. Louis University School of Medicine, 1914; member of the American Medical Association; died in July, aged 60.

Pattillo, Richard Starr, St. Petersburg, Fla.; Manitoba Medical College, Winnipeg, Manitoba, Canada, 1895; member of the American Medical Association and Illinois State Medical Society; formerly practiced in Chicago, where he was an instructor in clinical ophthalmology and otology at Northwestern University Medical School; died July 15, aged 80, of coronary thrombosis.

Reich, Samuel, Brooklyn; University and Bellevue Hospital Medical College, New York, 1920; on the staff of Crown Heights Hospital; died in Prospect Heights Hospital July 7, aged 52.

Reuscher, Leo George, Cincinnati; University of Cincinnati College of Medicine, 1911; also a graduate in pharmacy; served as district physician for the city board of health; died July 9, aged 67, of arteriosclerotic heart disease.

Rightor, Henry Haskell ✦ Helena, Ark.; Medical Department of Tulane University of Louisiana, New Orleans, 1904; specialist certified by the American Board of Otolaryngology; affiliated with Helena Hospital; died May 20, aged 72.

Robinson, Francis Arnold, Burlington, Mass.; Baltimore Medical College, 1894; school physician; died April 29, aged 81, of heart disease.

Ruch, Charles Henry ✦ Momence, Ill.; Indiana University School of Medicine, Indianapolis, 1926; health officer; affiliated with St. Mary's Hospital in Kankakee, where he died August 3, aged 54, of metastatic carcinoma following roentgen burns of the left hand.

Schodron, Robert Charles, Milwaukee; Marquette University School of Medicine, Milwaukee, 1928; member of the American Medical Association; died July 10, aged 50, of heart disease.

Schoendorff, Walter, Yonkers, N. Y.; Universität Köln (Cologne) Medizinische Fakultät, Köln, Prussia, Germany, 1923; member of the American Medical Association; died in Yonkers Professional Hospital June 27, aged 53.

Shepard, William Marshall, Adel, Ga.; Southern Medical College, Atlanta, 1892; member of the American Medical Association; served on the city council; died April 26, aged 81.

Shoss, Isadore Hyman, Houston, Texas; Baylor University College of Medicine, Dallas, 1945; member of the American Medical Association; died in Hermann Hospital July 8, aged 29, of rheumatic heart disease.

Simon, Louis Jacob ✦ Fond du Lac, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1908; served during World War I; in 1944 county deputy coroner; on the staff of St. Agnes Hospital; from 1934 to 1947 physician for the County Asylum and County Home; died June 26, aged 67, of coronary thrombosis.

Stump, Irwin C., Clendenin, W. Va.; University of Louisville (Ky.) Medical Department, 1894; member of the board of directors of Farmers' and Citizens' State Bank; died in a hospital in Charleston July 11, aged 79.

Tussing, Rudolph Frank, Chicago; Northwestern University Medical School, Chicago, 1936; member of the American Medical Association; served during World War II; affiliated with the Municipal Tuberculosis Sanitarium; died July 15, aged 44, of coronary thrombosis.

Van Urk, Thomas ✦ Miami Beach, Fla.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; member of the Michigan State Medical Society; for many years practiced in Kalamazoo, Mich., where he had been physician for the Home for the Aged; veteran of the Spanish-American War and World War I; died June 21, aged 76, of heart disease.

Wikoff, Clarence P., Bloomington, Ill.; Rush Medical College, Chicago, 1893; died July 9, aged 80.

Wright, Elva Annis, Houston, Texas; Northwestern University Woman's Medical School, Chicago, 1900; emeritus professor of obstetrics at Baylor University College of Medicine; member of the American Medical Association and American Trudeau Society; past president of the Texas Tuberculosis Association and Southern Tuberculosis Conference; for many years affiliated with Jefferson Davis Hospital; died July 18, aged 82, of ruptured aortic aneurysm.

Wright, Fred Snell, Bellaire, Ohio; Baltimore Medical College, 1910; fellow of the American College of Surgeons; served with the British and American armies during World War I; formerly member of the local board of health; died in Lawson General Hospital, Atlanta, May 21, aged 63.

FOREIGN LETTERS

LONDON

(From a Regular Correspondent)

July 24, 1950.

British Medical Association Annual Representative Meeting

The Annual Representative Meeting of the British Medical Association was held at Southport, Lancashire, July 13-17 and was attended by approximately 350 doctors from all parts of the British Isles. Dr. J. A. Brown of Birmingham was chairman. A civic welcome was extended by the mayor.

The first order of business was discussion of the relationship of the autonomous bodies to the representative body. Dr. Wishart of Bromley moved to confirm the composition and status of the General Medical Services (family doctors) Committee and the Central Consultants and Specialists Committee to require that their autonomous powers be specifically renewed by each successive annual representative meeting, but it was pointed out that these two main divisions of the profession might be used by a minister of health to divide and rule the profession; autonomy must not be allowed to become autocracy. Contrary to Council's report the meeting decided that the question of autonomy should be reexamined annually.

A WAR MEMORIAL

Dr. Guy Dain, chairman of the War Memorial Committee, said that its members had decided that the War Memorial should take the form of a fountain in the forecourt at British Medical Association headquarters with suitable sculptured statuary and, in addition, that there should be scholarships for the dependents of those who had given their lives in the war. It was decided that all doctors, whether members of the Association or not, who lost their lives in the war, should have their names included in the dedicatory inscription.

NATIONAL HEALTH SERVICE ACTS

Dr. Hale-White of Marylebone, London, moved: "That this meeting reaffirms its readiness to cooperate with the authorities in building up an efficient and smooth-working National Health Service but deeply regrets that all efforts in this direction during the past three years have been frustrated by the cavalier treatment accorded its representatives in their conversations and negotiations with the Minister."

He said there might be the impression that the profession was against any kind of National Health Service, but that was not so. It should be put on record that the profession continued its willingness to build up an efficient and smooth-working service, but he was none the less critical. He recalled some remarks by Mr. Bevan in the issue of the *British Medical Journal* on July 3, 1948, and he asked that the Minister's assurances be viewed in the light of after-events. In the two years since those words were written readers might now believe that the Minister had "plumbed the depths of insincerity" and they might also feel that they had the right to expect something better of a Minister of the Crown. For his own part he did not believe that the Minister had ever the slightest intention of cooperation once he got the doctors "in the bag." In fact, he did not believe that the Minister knew how to cooperate; it was not in his make-up. The method of dictation by the Minister and subservience by the profession had been tried for two years—two years too long—and had failed, as they all knew it would. Among doctors, especially general practitioners, it had produced distrust and cynicism. The motion was carried unanimously.

PROGRAM ON REFORMS

Mr. Langston, a surgeon, of Winchester, moved: "That this meeting considers the time long overdue when the Association should formulate a detailed program of reforms the profession desires to be adopted in relation to the National Health Service and instructs the Council to draw up such a list forthwith for submission to and discussion by branches and divisions."

He maintained that the service was being undertaken by a medical profession which was frustrated, overworked, tired and disillusioned. There was great dissatisfaction in all branches in various degrees, greatest among general practitioners.

The Association had not yet published any detailed program of reform and urged for the formulation of a detailed program.

Dr. A. V. Russell of Wolverhampton pointed out that when the doctors were induced, much against their will, to enter the service it was with the understanding that they would be able to shape it to their own desires. They had been assured of amending legislation. They were assured that the amending act would not be tabled without prior consultation, whereas it came before the House of Commons without any consultation at all and had not embodied anything which altered the main position at all. One of the main things which should be considered was the curtailment of the overriding powers of the Minister.

Other speakers felt that there should be a greater representation of family doctors of all bodies administering the service. Owing to this lack, they felt a sense of frustration. They did not think that the public was satisfied—partly owing to the enormous increase of private bed costs. The service was being saddled with an enormous burden of bureaucracy, with extravagant lay administration.

The motion was carried unanimously.

AMENDING ACTS COMMITTEE

Dr. Barbara Woodhouse of Harrow moved that a standing committee should be set up, as the National Health Service "child" was born "on the wrong side of the blanket." In order that the health services might be got into a healthy condition, it would be necessary to correct abnormalities by the formation of such a standing committee.

Other speakers pointed out that the government machine had increased tremendously and had now become overriding and topheavy. All Ministry of Health regulations should be carefully scrutinized.

There was a great deal of support for some change in the act from members of Parliament. The present act could be put right only by a new act.

The motion was carried.

POSITION OF THE FAMILY DOCTOR

Dr. Wand, chairman of the General Medical Services Committee (representing all family doctors) said that the Minister of Health, who had accepted the Spens report previously, had made it clear at their last interview that he did not regard this report as necessarily a continuing factor. They had always been aware of the possibility of unilateral action on the part of the Minister. The betterment factor, or cost-of-living bonus, which they had requested should be 70 per cent, was at present only about 40 per cent, but 70 per cent was now too low and it should be nearer 100 per cent. Although the Minister had expressed a good deal of sympathy, the trouble at the moment was with the Treasury and the Chancellor.

What was the financial position of general practitioners today? According to the Doctor's Remuneration Tables prepared by the government, at the lower end of the scale 36.4 per cent were earning under $2,800 net a year. The time it took to qualify as a doctor, the cost of education and the fact that he did not earn money until he was 23 or 24 years of age must all be taken into account. At the upper end of the scale the general practitioner compared badly with the specialist. The whole general practitioner group was lower than the specialist group. One Sunday paper worked out that the service cost $26 a year for each person. But the general practitioner's share was about 0.03 a week—equal to a little more than one cigaret, or one cigaret and a match. In these days of attractive specialties it was more than ever necessary that there should be a first class general practitioner service, but as it was it was likely to be increased by registrars who wanted to get into consultant practice and for whom there were no places.

PROVISION OF DIAGNOSTIC FACILITIES

Dr. F. M. Rose (Preston) moved that the representative body reiterate its demand for the provision of x-ray and laboratory facilities to be made directly available for general practice, either in hospital or elsewhere.

NATIONAL FORMULARY

Dr. W. Radcliffe moved that the approximate cost of each prescription in the National Formulary should be printed in future editions.

Dr. A. B. Davies said that there had undoubtedly been a vast increase in the number of prescriptions under the National Health Service Act, and he suggested that at least some of the responsibility for this rested on the Minister, who, at the inception of the new service had promised the public that the sky should be the limit.

PROVISION OF MEDICINE FOR PRIVATE PATIENTS

A speaker said it was wrong to deprive a certain section of the community of something for which they had paid. Private patients paid just as much as anyone else by their contributions and more than others by way of taxation. He asserted the real reason for not allowing free medicine and appliances to private patients was that the Government was afraid to allow private practice to compete on equal terms with the National Health Service.

CERTIFICATES FROM OTHER THAN MEDICAL PRACTITIONERS

Dr. J. A. Gorsky (Westminster and Holborn) asked the meeting to express its disquiet at the absolute power possessed by the determining authority under section 43(3) of the National Insurance Act 1946, and clause 2(1) of S. I. 1948 no. 1175, to accept certificates or other evidence of incapacity for work for sickness benefit claims from persons other than registered medical practitioners. He declared that such procedure did not allow for safeguards against abuse, lowered the status of medical practitioners, and was inconsistent with section 37 of the Medical Act of 1858.

It would, be said, be a tragedy not only for the profession but also for the nation which it served if the public were left with the impression that, once the matter of remuneration were settled, all would be well with the National Health Service. The medical profession was threatened with encroachments on the ethical and professional freedom of its members and could not tolerate any further degradation of medicine into a state monopoly.

PRIVATE PATIENTS IN HOSPITALS

Dr. P. J. Gibbons (Liverpool), in moving "That this meeting draws attention of the Ministry to the excessive charges for private patients in hospitals and considers that steps should be taken to review these charges in accordance with the promise of the Minister," said that when medical practitioners entered the National Health Service two years ago they did so in the belief that private practice would form an integral part of the service but that position had been gradually undermined by the policy of the Ministry. The cost of beds for private patients in hospital had been increased to such an extent that it was almost impossible for any except the most wealthy persons to have private treatment in hospital. A definite charge should be fixed, to apply to all private beds in hospitals, and that charge should be a moderate one.

GENERAL PRACTITIONERS AND THE HOSPITAL

The interim report of the Council, under the heading "The General Practitioner and Hospital Work," was received, and recommendations were moved calling for the retention of the smaller family doctor and cottage hospital for practitioners. The following recommendations were finally adopted:

The smaller family doctor and cottage hospital should be retained by the general practitioner and, in addition, certain wards in district hospitals should be set aside for treatment of patients by general practitioners.

Clinical assistantships posts should be made available for educational purposes, allowing for two year periods of training in any particular specialty and, also, for short periods in two or three special departments.

Part time appointments should be made and held by general practitioners.

In rural areas the appointment of part time general practitioner-specialists should be retained and encouraged.

ARGENTINA

(From a Regular Correspondent)

BUENOS AIRES, July 24, 1950.

Alastrim

In the last three years many cases of alastrim appeared in different zones of Paraguay, Argentina and Chile. An intensive campaign against smallpox has been carried out in the Argentine republic, a certificate of vaccination being necessary even to travel from one town to another. This measure was canceled when the epidemic abated, but some cases of alastrim are still observed from time to time, as in the city of Nove de Julio, where it was necessary to close cinemas, clubs and bars for twelve days. In Chile, 2,191 cases already have been observed, and a Chilean-Argentine committee was formed to study the best measures to prevent transmission of the disease from one country to the other.

Dr. R. Palacios, chief of the Virus Department of the Bacteriological Institute of Chile, has been working on the alastrim virus in the Bacteriological Institute "Carlos Malbrán" in Argentina.

Strike of Sanitary Workers

In hospitals, clinics and cemeteries of Santiago, Chile, a general strike of more than 20,000 employees affected 60,000 patients. The Ministry of Health declared the strike illegal and criminal and employed all possible resources to assist needy persons.

Lectures on Physiology

Dr. S. R. M. Reynolds, from the Department of Embryology of Carnegie Institution, Baltimore, was invited by the University of Montevideo to work there for two months. He carried out investigations in the Department of Obstetric Physiology, which develops its activity in the Chair of Obstetrics in association with the Institute of Physiology. Dr. Reynolds delivered some lectures on physiology of the uterus, and at the close of his visit the University of Montevideo conferred on him the degree of Honorary Professor, at the suggestion of the medical school. Dr. Reynolds also visited Buenos Aires, where he stayed for two days.

CORRESPONDENCE

CANCER OF THE LUNG

To the Editor:—The rapid rise in the frequency of lung cancer during the past thirty years has become the subject of a great deal of critical study and speculation. Although many investigators still maintain that this increase is merely apparent and the result of a shift in the age composition of our population in recent decades, better diagnostic facilities and a greater awareness of the medical profession for this particular cancer, others believe they have proved that this development is at least in part real and caused by the advent of new cancerigenic factors in our environment. This concept receives some indirect support from the fact that the majority of new occupational cancers discovered during the past half-century affect the respiratory system and can definitely or tentatively be traced to chemical and physical agents (chromates, asbestos, arsenicals, tar fumes, radioactive gases and dust, nickel carbonyl, isopropyl oil or lubricating oil), some of which also may form a part of our general environment. However, since the total number of these environmental respiratory cancers forms only a small fraction of the total number of such lesions, other explanations were sought during the past three decades and an astonishing number and variety have been presented in attempts to account wholly or mainly for the production of lung cancer and its recent rise in frequency. Some investigators claimed that the influenza epidemic of World War I was causally related to this phenomenon. Others alleged that the pollution of the air with sulfur dioxide or carbon monoxide from industrial and domestic sources accounted for the increase in lung cancer. A third group proposed that the rapid recent increase in tarred roads with the resulting inhalation of tar dust or of exhaust fumes from gasoline and Diesel engines might be responsible for this development. Then there were those who were satisfied with incriminating any type of respiratory irritant, such as nondescript dust, gases or fumes. The most recent phase in this search for "the" cause of cancer of the lung is represented by the suggestion that excessive smoking, especially of cigarets, and the inhalation of hot tobacco fumes containing tobacco tar tells all or most of the story of respiratory cancerigenesis (Schrek, R.; Baker, L. A.; Ballard, G. P., and Dolgoff, S.: Tobacco Smoking as an Etiologic Factor in Disease. I. Cancer, *Cancer Research* **10**:49, 1950. Wynder, E. L., and Graham, E. A.: Tobacco Smoking as a Possible Etiologic Factor in Bronchiogenic Carcinoma, *J. A. M. A.* **143**:329 [May 27] 1950. Levin, M. L.; Goldstein, H., and Gerhardt, P. R.: Cancer and Tobacco Smoking, ibid. **143**:336 [May 27] 1950). It is shown in these investigations that, statistically, the percentage of excessive smokers of cigarets is significantly higher among persons with lung cancer than among those with other malignant or nonmalignant diseases. It is somewhat disconcerting to note, however, that one group of investigators (Wynder and Graham) included all types of smoking (cigaret, cigar and pipe) with equal weight in the analysis, while the other group (Levin, Goldstein and Gerhardt) stated that only cigaret smoking is statistically related to lung cancer. Since no other environmental factor has been considered in any of these studies, the incorrect impression may be produced that smoking apparently represents the only important cause in the production of lung cancer. There can be no denying that excessive smoking may become a serious liability to health, aside from its possible relationship to the possible development of lung cancer. The actual epidemiologic and experimental evidence linking lung cancer to exposure to tar dust or fumes (the probable cancerigenic agent in tobacco tar) leaves much to be desired. In fact, even with the use of highly carcinogenic coal tar introduced by various routes into the trachea or lung of experimental animals it has been difficult or impossible to cause cancer of the lung. That tobacco tar is a much weaker cancerigenic agent than coal tar is a well demonstrated fact. In view of these considerations, it seems advisable not to close our eyes to the possible or probable existence of other cancerigenic agents in any future search for the causes of cancer of the lung, larynx and nasal sinuses.

AUSTIN V. DEIBERT, M.D., Chief Cancer Control Branch, National Cancer Institute, Bethesda 14, Md.

SALT-FREE DIET

To the Editor:—The rapidly widening use of the salt-free diet for hypertension will doubtless bring further accurate reports of results, like the recent one of Kert and associates (THE JOURNAL, June 24, p. 721). The following comments are based on an experience of several thousand cases during thirty years:

1. Refractory cases are apt to be more numerous among clinic than private patients, and some adverse reports have been based on such material. It should be noted that cases for diet treatment are taken indiscriminately, without exclusion on account of severity or complications. Statistics of surgical treatment are based on carefully screened cases. Most of those selected and many of those rejected by surgeons will respond to correct diet.

2. The decisive test is not initial benefit (which might be ascribed to hospitalization, psychic or other influences) or apparent failure over several weeks or months. If patients like those of Kert and associates are followed with strict diet for a number of years, the favorable cases will maintain or extend their improvement, and the majority of the initially refractory cases will show either slow improvement or at least an arrest of the usual progressiveness. No opponent has ever observed this treatment of a chronic disease long enough to learn these results.

3. As shown by Allen and Sherrill in 1922 (*J. Metab. Research* **2**:429-545) nephritic cases are not as thoroughly controllable as those of essential hypertension; also it is necessary occasionally but not often to add a limited amount of salt to prevent uremia.

4. Existing retinitis, angina and other complications are frequently but by no means always relieved by diet. Also, no known treatment can entirely obviate the consequences of preexisting arteriosclerosis, in the form of fatal coronary or cerebral accidents. But the specific effect of the diet is proved by its unique prevention of complications. Whereas over 50 per cent of persons with essential hypertension ordinarily die in congestive failure, and retinitis, claudication, angina and uremia are frequent, I have never witnessed a single onset of any of these complications in a patient on continuous saltless diet. Aside from rare "malignant" cases, this rule holds not only for the initially favorable group but for those which have appeared refractory, also for patients who show incipient signs of any of these conditions on beginning treatment.

5. Combined experimental and clinical evidence now establishes the etiologic role of salt excess and indicates correction of prevalent abuses of salt as a public health measure to check this leading cause of death (Allen, F. M.: *Nutrition Rev.* **7**:257 [Sept.] 1949).

FREDERICK M. ALLEN, M.D., New York.

OCCURRENCE OF DEAFNESS IN NEOMYCIN THERAPY

To the Editor:—Although more than a year has passed since Waksman announced the discovery of neomycin, clinical trials in tuberculosis seem to have been delayed by the difficulty in producing a potent, nontoxic preparation containing a single neomycin (G. L. Hobby, T. F. Lenert and N. Dougherty, *Ann. New York Acad. Sc.* **52**:775-781 [Dec. 14] 1949).

A few months ago we obtained a supply of neomycin containing 200 Waksman units per milligram, which was said to be a single neomycin as determined by paper chromatograms. Earlier studies with this material had revealed that it was effective against experimental tuberculosis produced in guinea pigs by inoculation with streptomycin-resistant tubercle bacilli and that slight renal damage was its only demonstrable toxic effect (A. G. Karlson, J. H. Gainer and W. H. Feldman, *Dis. of Chest* **17**:493-502 [May] 1950).

This material was given to 6 patients, 5 of whom had tuberculosis due to streptomycin-resistant tubercle bacilli and 1 of whom had tuberculosis and extensive carcinomatosis. The dose varied from 0.25 to 1.0 Gm. given every twelve hours for four to seven weeks. Studies of renal function showed some temporary damage in all 6 cases. Of much greater significance was the sudden development of partial deafness in 4 of the 6 patients during the fourth to the sixth week of treatment. This varied from slight to severe and persisted without change after the administration of neomycin had been discontinued.

Roentgenograms of the thorax of 1 patient who had tuberculous bronchopneumonia of a few weeks' duration showed almost complete resolution of the disease in a period of twenty-eight days, during which she received 42 Gm. of neomycin. Two other patients with acute exudative pulmonary lesions had no signs of improvement after use of a smaller dose of the drug.

Whether the deafness was produced by the neomycin itself or by some impurity could not be determined. However, since other similar preparations of neomycin are being made available for clinical trials, it seemed wise to call attention to this serious toxic reaction by means of this preliminary communication.

D. T. CARR, M.D., and H. A. BROWN, M.D.,
Rochester, Minn.
K. H. PFUETZE, M. D.,
Cannon Falls, Minn.

WATER RETENTION FOLLOWING CORTISONE THERAPY

To the Editor:—Dr. Archer's letter (*J. A. M. A.* **143**:570 [June 10] 1950) was of interest to us as we have been treating patients with cirrhosis of the liver with cortisone with a fixed regimen in a metabolic ward. Cortisone, 100 mg., has been given for 18 days to 3 patients. These patients all retained water during treatment, and their livers became extremely hard and somewhat larger than during the pretreatment period. When cortisone therapy was stopped, the livers returned to previous size and consistency within 10 days. Liver function tests (sulfobromophthalein sodium, bilirubin, cholinesterase activity, gamma globulin, thymol turbidity, zinc sulfate turbidity, cephalin-cholesterol flocculation, prothrombin time) showed no remarkable changes. Unfortunately, we were unable to take liver biopsy specimens from these patients. We suspect the swelling to be due to water retention, but the possibility exists that fat deposition occurred. There was no change in fasting blood glucose levels during or after cortisone therapy in these patients.

ROBERT A. CHAPMAN, M.D.
ROBERT M. KARK, M.R.C.P. (London), Chicago.

LIPOMELANIC RETICULOSIS

To the Editor:—I was interested in the article that appeared in THE JOURNAL July 15, 1950 (page 957) "Lipomelanic Reticulosis" by Drs. Agress and Fishman of California. It should be emphasized that most dermatologists have observed the generalized lymph adenopathy associated with chronic dermatoses. I also feel that credit should be given to Dr. Elliott Hurwitt, whose excellent paper appeared in *The Journal of Investigative Dermatology* in August 1942. He called the condition "dermatopathic lymphadenitis," or focal granulomatous lymphadenitis associated with chronic generalized skin disorders. He reported a series of 12 cases carefully studied with excellent microscopic descriptions of the lymph nodes involved.

NEVILLE KIRSCH, M.D., Hartford, Conn.

To the Editor:—In their article entitled "Lipomelanic Reticulosis, Agress and Fishman describe the disorder as a "harmless syndrome." Lest the readers of THE JOURNAL be led to believe that this condition is always benign, it may be well to point out that S. M. Bluefarb and J. R. Webster (*Arch. Dermat. & Syph.* **61**:830-841 [May] 1950) recently described 2 cases of lipomelanotic reticulosis which developed into mycosis fungoides.

JOHN M. SIEGEL, M.D., Allentown, Pa.

EPIDEMIOLOGISTS IN HOSPITALS

To the Editor:—May I take this opportunity to enlist your help in promoting one of the objectives of the Dysentery Registry, namely, the appointment of an epidemiologist to the staffs of hospitals. Each year at this time we initiate our regular "Prevent Dysentery" program, and for 1950 we are stressing the importance of the hospital epidemiologist. As you know, intramural outbreaks of various types frequently occur in our hospitals but are poorly managed or are inadequately studied.

JOSEPH FELSEN, M.D., New York.

WOMEN PHYSICIANS IN THE NAVY

To the Editor:—I wish to correct a certain statement made in Washington News in the August 5, 1950 issue of THE JOURNAL. In the paragraph on page 1263 which deals with women physicians in the services, the statement is made, regarding women physicians in the Navy, ". . . they remain line officers." This statement is incorrect. Women physicians in the Navy are in the WAVE Corps, but they are not line officers; they wear the uniform and insignia of a medical officer and serve within the structure of the Medical Department and the Medical Corps.

C. A. SWANSON, Rear Admiral,
Surgeon General, U. S. Navy.

LABELING

To the Editor:—The editorial "Read the Labels" in THE JOURNAL, July 8, page 899, suggests to me a method of determining how medicaments should be injected. Labels with pictures of vein, muscle or skin in cross section would indicate to all physicians the method of injection or injections available with each drug solution.

One point not covered in the editorial is the difficulty in reading the small print on some labels. The Chinese proverb about the equivalent of one picture would be most apt here.

GOTTLIEB HELFERN, M.D., New York.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACT

Massage: Use of Electric Vibrator Not Practice of Massage.—The plaintiff filed suit against the Florida board of massage and others for a declaratory decree interpreting the Massage Registration Act of 1943. From a decree in favor of the plaintiff, the defendant appealed to the Supreme Court of Florida, Division A.

The Florida statutes relating to massage provide in part as follows: "As the following subjects and methods of treatments besides study of underlying principles of anatomy and physiology are generally included in a regular course of study by a recognized and accredited school of massage or like institution, viz.: The art of body massage, either by hand or with any mechanical or electrical apparatus for the purpose of body massaging, reducing or contouring, the use of oil rubs, salt glows, hot and cold packs, tub, shower, sitz and similar baths, cabinet baths, excluding fever therapy, therefore under the meaning of this chapter the term 'masseur' or 'masseuse' shall be deemed to be a person who practices, administers or teaches all or any one or more of the above named subjects and methods of treatments."

The plaintiff's business involved the use of mechanical equipment, electrically operated and applied to the human body for slenderizing purposes. The equipment so used consisted of a hip chair, arm chair, hobby horse, foot table, couch composed of three adjustable panels, and a cushion. The plaintiff testified that the equipment did not massage the human body but set up or caused a gentle vibration; that there is no massage of the human body by hand, and that her business did not involve the use of oil rubs, salt glows, hot or cold packs, tub, shower, sitz or similar baths, or cabinet baths, nor any disrobing of the customer, nor the use of towels, except paper towels for the head rest, on the couch and on the platform of the foot table.

The trial court found that the term "massage" has a well-defined meaning; that the generally accepted meaning of the term "massage" is a "rubbing, stroking or kneading" of the body; that the electrical equipment used by the plaintiff causes, through electrical impulses or by some other means, a vibration to the body, but that "said equipment does not massage, rub, stroke or knead the body," and it therefore decreed that the plaintiff was not engaged in the practice of massage as contemplated by the Florida statutes.

The defendant, on appeal, contended that the trial court erred in applying the general definition of the word "massage" in its interpretation of the statute and that the legislature, by a 1947 amendment, which added to the definition the words "electrical apparatus" and "reducing or contouring" thereby expressly defined the term "massage" to include such equipment as that used by the plaintiff.

With this contention we cannot agree, said the Supreme Court of Florida. The statute regulates the practice of "the art of body massage, either by hand or with any mechanical or electrical apparatus for the purpose of body massaging, reducing or contouring. . . ." It is our opinion that, by appending the term "electrical apparatus" as a descriptive phrase to "the art of body massage," the legislature has clearly limited such electrical apparatus to that which rubs, strokes or kneads the body, according to the general definition of the term "massage." It is true, the Supreme Court continued, that the legislature has also included in its definition other practices, ordinarily found in a massage establishment, which do not involve a rubbing, stroking or kneading of the body, such as hot and cold packs, tub, shower, sitz, and cabinet baths, but this merely reinforces our opinion, since the legislature could have added "electrical apparatus" to this group of practices not involving an actual massage of the body.

Moreover, continued the court, it is provided in the statutes that the minimum educational requirements for a registered masseur or masseuse are 100 hours of physiology, 100 hours of anatomy, 100 hours of massage, 200 hours of hydrotherapy and 100 hours of hygiene and practical demonstration in an approved massage school. Since by no stretch of the imagination can it be said that a knowledge of such subjects is essential to the purely mechanical operation of the electrical equipment here involved, or that such knowledge would add to the competency of the operator of such equipment, we think it is clear, the Supreme Court concluded, that the legislature did not intend to include the use of the electrical equipment here involved in its definition of a masseur or masseuse. Accordingly the judgment of the trial court in favor of the plaintiff was affirmed.—*Florida Board of Massage v. Underwood, 45 So. (2d) 184 (Fla., 1950).*

Malpractice: Resident's Liability for Negligence During Operation.—The plaintiff sued for damages caused by the alleged malpractice of the defendant physician. From a judgment in favor of the plaintiff which was reversed by the appellate court (*Valdez v. Hankins,* 211 P. (2d) 6; *J. A. M. A.* **142**:1315 [April 22, 1950]), the plaintiff appealed to the Supreme Court of California.

Having been advised that an enlarged lymph gland in the axilla should be removed and examined microscopically for determination of whether or not it was malignant, the plaintiff entered the hospital and submitted to the suggested operation. The gland was removed and sent to the hospital laboratory for an analysis. While the plaintiff was still under anesthesia, the head nurse announced that the laboratory finding was carcinoma. The decision was then made to proceed at once and remove the plaintiff's right breast. This operation was performed. However, just prior to the plaintiff's removal from the operating room, after the completion of the operation, the laboratory announced that it had made a mistake in its diagnosis and that the laboratory then thought the condition was "Hodgkin's disease or a possible lymphoma."

The defendant was a resident physician at County General Hospital assigned to the surgical services of which Dr. Percy (who died prior to this trial) was chief, and it was his duty to assist Dr. Percy as directed. Except as assistant to Dr. Percy, the defendant had no connection with the plaintiff's case or her operation. Although Dr. Percy had directed the defendant to perform the operation, Dr. Percy himself had done a great deal of assisting and had performed certain difficult parts of the operation alone.

The defendant contended that, if there was negligence, it was not attributable to him, since the evidence showed that he was assigned by the hospital authorities to assist during the operation under the direction and control of Dr. Percy and that it was his duty to follow the directions given to him by Dr. Percy during the course of the operation. The defendant testified that he operated under the direction and with the assistance of Dr. Percy, who did some of the more difficult sections. The fact that the defendant performed the operation, with or without assistance or direction, stands uncontradicted, pointed out the Supreme Court. Since he was a co-actor, he was a joint tortfeasor and liable to the plaintiff for the entire damage ensuing from the negligent act. The Supreme Court concluded, therefore, that the evidence was sufficient to support the findings of negligence made by the jury and the judgment of the trial court was accordingly affirmed.—*Valdez v. Percy et al., 217 P. (2d) 422 (Calif., 1950).*

Admissibility in Evidence of Results of Chemical Tests for Intoxication.—The defendant was charged with operating a motor vehicle on the highway while under the influence of intoxicating liquor. From a judgment of conviction, he appealed to the Supreme Court of Indiana.

The defendant contended that the trial court erred in overruling his motion to suppress the results of a test made on him by means of a drunkometer. After considering all the evidence, the Supreme Court held that, since the defendant voluntarily submitted to the test after being arrested, the results thereof were properly admitted even though no formal charge had yet been preferred. The judgment of conviction was affirmed. —*Willennar v. State, 91 N. E. (2d) 178 (Ind., 1950).*

CURRENT MEDICAL LITERATURE

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in Continental United States and Canada for a period of five days. Three journals may be borrowed at a time. Periodicals are available from 1939 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

19:289-332 (April) 1950

*Importance of Normal Pathways of Tumor Spread in Establishing Methods of Treatment for Uterine Cancer. A. M. Arneson.—p. 289.
Surgical Problem of Advanced Gastric Cancer. A. Brunschwig.—p. 295.
Carcinoma of Pharynx and Larynx. L. H. Clerf.—p. 297.
Radiation Therapy of Lymphomas. R. M. Caulk.—p. 300.
Cancer of Colon and Rectum: Factors Influencing Greater Curability. H. E. Bacon and L. F. Sherman.—p. 310.

Normal Pathways for Tumor Spread in Uterine Cancer.—According to Arneson the most frequent point of origin for cancer of the cervix is at the junction of columnar and squamous epithelium. Spread from that location is by direct growth along pathways of least tissue resistance, and by dispersion chiefly through the lymphatic system. Considerable variation exists in the behavior of different cervices involved with cancer. In some instances there may be piling up of tumor cells on the surface to produce sessile or partially pedunculated cauliflower-like masses with a minimum of invasion. There are instances in which the cervix is expanded into a hard nodular form by virtue of growth into cervical tissue beneath a relatively intact mucous membrane. Endocervical varieties producing a worm-eaten type of lesion would seem to fall into the more invasive group. The tumor may assume a superficial character and be distributed rather thinly, but widely, over the mucous membrane. Variations in gross forms may be associated with different consequences in the natural history of the disease. Virchow noted that tumors growing outward toward the observer present a more favorable clinical course than those growing inward. The invasive tumors may be more apt to undergo early dispersion because malignant cells can more promptly reach points rich in lymphatic vessels. Infiltrating tumors because of their tendency to grow beneath an intact mucous membrane are late to ulcerate and consequently do not produce clinical symptoms as promptly as do the more spongy and friable everting types. As a result, the invasive types of cervical cancer are usually well advanced by the time diagnosis is established. This fact would in part explain the difference in end results for everting and infiltrating forms which are shown in 224 cases. A difference in prognosis can be shown for the various gross types found within the same clinical stage. The difference in prognosis is not pronounced in stage 1, because a high percentage of all types survive. In the more advanced stages the survival rate is low for all varieties. In stage 2, however, there is a definite difference in the five year results for everting and infiltrating forms. The better prognosis shown for everting types must be due to a lesser incidence of dispersion. The author discusses spread of cancer by direct growth and spread by dispersion, the latter occurring chiefly through the lymphatics. Data on lymphatic dispersion have been obtained from autopsy material and from surgical procedures. One of the most detailed studies of tumor spread is that by Henricksen in autopsies on 356 cases of cervical cancer and 63 cases of endometrial cancer. Knowledge of the spread of cervical cancer may make possible the detection of cases apt to resist irradiation and better suited to surgical treatment.

American J. Digestive Diseases, Fort Wayne, Ind.

17:137-172 (May) 1950

Pancreatic and Gallbladder Functions in Peptic Ulcer and Chronic Ulcerative Colitis. W. J. Snape and M. H. F. Friedman.—p. 137.
Clinical and Roentgenologic Findings in Steatorrhea of Varying Causes. C. J. Bjerkelund and O. W. Husebye.—p. 139.
Approach to Problem of "Epinephrine Fastness." F. F. Yonkman, L. Levinson and M. S. Segal.—p. 149.
Comparative Capacities of Absorptive Agents for Endogenously Produced Toxic Chemicals. G. J. Martin and S. Alpert.—p. 151.
Gastrointestinal Symptoms Resulting from Cardiac Medications. F. M. Groedel and M. Miller.—p. 154.
History of Rectal Medication and Its Indication in Cardiovascular Disease. M. Miller and F. M. Groedel.—p. 157.
Tendency to Rumination. J. N. Dambassis.—p. 159.
Dietary Principles in Digestive Diseases. A. C. Johnson.—p. 161.

American Journal of Ophthalmology, Chicago

33:673-846 (May) 1950

Histochemical Localization of Glucuronidase in Ocular Tissues and Salivary Glands. B. Becker and J. S. Friedenwald.—p. 673.
Dystrophies of Cornea. E. L. Goar.—p. 674.
Hereditary and Constitutional Dystrophies of Cornea. W. B. Clark.—p. 692.
Action of Lutazol and Ophtazol in Treatment of Trachoma. V. Tsopellas.—p. 704.
Experimental Study of Reticulo-Endothelial Function of Eye with Special Reference to Its Role in Chemotherapeutic Action of Sulfonamides. G. Lugossy.—p. 709.
Sulfonamides and Penicillin in Trachoma. A. A. Siniscal.—p. 715.
Fingerprintlike Lines in Cornea. DuP. Guerry III.—p. 724.
Ocular Pathology of Diabetes. S. Gartner.—p. 727.
Attempt to Influence Corneal Wound Healing by Local Application of Certain Amino Acids. A. J. Schaeffer.—p. 741.
Congenital Levator and External Rectus Muscle Internuclear Associated Reflex. E. B. Spaeth.—p. 751.
*Glaucoma and Orally Administered Belladonna. E. V. Ullman and F. D. Mossman.—p. 757.
Choice of Operation in Acute Glaucoma Secondary to Swelling of Lens. P. Sternberg and S. J. Meyer.—p. 763.
Flicker Fusion Fields: I. Effect of Age and Pupil Size. P. W. Miles.—p. 769.
Headache as Symptom of Visual Disability. C. B. Foster.—p. 773.
Myopia, Vitamin A and Calcium. J. B. Feldman.—p. 777.
Albinism: Report of Unusual Family. A. Wallner and M. C. Rudens.—p. 785.

Glaucoma and Orally Administered Belladonna.—Ullman and Mossman report 6 cases in which extract of belladonna or tincture of belladonna was given for gastrointestinal complaints, such as duodenal or peptic ulcers, ulcerative or spastic colitis, hyperacidity or psychosomatic complaints centered in the gastrointestinal tract. The patients were in the glaucoma age group, between 38 and 68, and 5 of the 6 had narrow filtration angles. Since the authors did not examine any of these patients before the medicament was given, no statement can be made on whether the drug or a specific dosage had caused glaucoma, but in all cases the taking of the drug was followed within a few days to several weeks by ocular symptoms, of which the patient had not previously been aware. None of the physicians who had prescribed the drug had given any thought to the possibility of ocular consequences or had questioned the patients as to possible past eye disease or eye treatment; nor did it occur to the authors prior to their first case to question the patients as to medicaments that had been used prior to the eye

examination. In some cases of this nature patients may have been treated for glaucoma without discovery of the fact that belladonna medication had previously been given. The authors cite figures which suggest that approximately one fourth of their cases of primary glaucoma were induced or aggravated by the administration of belladonna. They discuss mydriatic glaucoma due to topical use of mydriatics, and they point out that the literature contains no reports correlating glaucoma with orally administered belladonna.

American Journal of Psychiatry, New York

106:801-880 (May) 1950. **Partial Index**

Fate of 395 Mild Neuropsychiatric Cases Salvaged from Training Period and Taken into Combat. W. L. Sharp.—p. 801.
Psychiatry and Rehabilitation in Military Setting. H. Wexler.—p. 812.
Effect of Trimethadione (Tridione) and other Drugs on Convulsions Caused by Di-Isopropyl Fluorophosphate (DFP). H. E. Himwich, C. F. Essig, J. L. Hampson and others.—p. 816.
Continuous Sleep Treatment: Observations on Use of Prolonged, Deep, Continuous Narcosis in Mental Disorders. J. S. Clapp and E. A. Loomis Jr.—p. 821.
Clinical Management of Mentally Retarded Child and Parents. R. A. Jensen.—p. 830.
Program for Orientation in Child Psychiatry. J. A. Rose.—p. 834.
Postgraduate Psychoanalytic Training Program: Its Evolution, Principles and Operation at New York Medical College. A. Gralnick. —p. 841.
Who Goes to a Psychiatrist? Report on 100 Unselected, Consecutive Cases. N. K. Rickles, J. J. Klein and M. E. Bassan.—p. 845.
Role of Psychiatrist as Consultant. J. G. N. Cushing.—p. 861.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

63:629-796 (May) 1950

Chest Lesions Often Confused Roentgenographically with Primary Cancer of Lung. P. C. Swenson and R. H. Leaming.—p. 629.
*Roentgenographic Appearance of Interatrial Septal Defect: Report of 12 Cases. R. F. Healey, J. W. Dow, M. C. Sosman and L. Dexter. —p. 646.
Value of Tannic Acid Enema and Post-Evacuation Roentgenograms in Examination of Colon. A. C. Christie, F. O. Coe, A. O. Hampton and G. M. Wyatt.—p. 657.
Roentgenographic Demonstration of Rokitansky-Aschoff Sinuses of Gallbladder: Report of Case. B. C. Bean and G. J. Culver.—p. 665.
Roentgen Pelvimetry by Differential Divergent Distortion. I. Isaacs. —p. 669.
Accurate Isometric Roentgen Pelvimetry in Erect Posture. H. C. March.—p. 677.
Roentgen Irradiation of Desoxyribosenucleic Acid: I. Mechanism of Action of Irradiation in Aqueous Solution. G. Limperos and W. A. Mosher.—p. 681.
Id. II. Physicochemical Properties of Desoxyribosenucleic Acid from Irradiated Rats. G. Limperos and W. A. Mosher.—p. 691.
End Results of Radiotherapy of Cancer of Tongue. J. Baud.—p. 701.
End Results of Treatment of Cancer of Tongue. E. Berven.—p. 712.
Treatment of Cancer of Tongue. S. Cade.—p. 716.
End Results and Treatment of Cancer of Tongue. B. W. Windeyer. —p. 719.
Technique and Results of Treatment of Cancer of Tongue with 10 Gram Radium Beam Unit. C. A. P. Wood.—p. 727.

Roentgenographic Appearance of Interatrial Septal Defect.—Healey and co-workers report roetgenographic and circulatory changes in 12 patients between the ages of 10 and 56 years with interatrial septal defect. Significant roentgen observations included cardiac right atrial and right ventricular enlargement and dilatation and hyperactivity of the pulmonary artery. The aorta appeared small in 3 cases. Left atrial enlargement was not observed. Posterior enlargement of the right ventricle simulated that of the left in 7 cases. A correlation of the roentgenographic appearance with hemodynamic changes revealed that a small left to right shunt through an atrial defect did not produce recognizable changes in the heart or pulmonary artery. A large shunt usually resulted in decided changes, but an exception was noted. Small interatrial shunts associated with severe pulmonic hypertension were indistinguishable roentgenographically from large interatrial shunts without pronounced pulmonic hypertension. Aneurysmal dilatation of the pulmonary artery, usually associated with Lutembacher's syndrome, was observed at necropsy in 1 case without a lesion of the mitral valve. Roentgenographic appearance in 3 additional patients with cor pulmonale, the Eisenmenger complex and isolated ventricular septal defect, respectively, was identical with or closely resembled an interatrial septal defect, making differential diagnosis on this basis difficult. The absence of enlargement of the hilar and peripheral branches of the pulmonary artery in pulmonic stenosis serves to distinguish this anomaly from interatrial septal defect with a fair degree of accuracy, but 1 of the authors' cases was erroneously diagnosed from the roentgenogram as mild pulmonic stenosis because the main pulmonary artery was dilated without a corresponding dilatation of the hilar or intrapulmonary branches. The tetralogy of Fallot does not resemble an interatrial septal defect.

Archives of Ophthalmology, Chicago

43:793-966 (May) 1950

Cyclodialysis: Its Mode of Action: Histologic Observations in Case of Glaucoma in Which Both Eyes Were Successfully Treated by Cyclodialysis. O. Barkan.—p. 793.
Transplantation of Lacrimal Glands in Man and Rat; Effect of Injury of Lacrimal Duct in Rat: Clinical and Experimental Study. M. Vannas.—p. 804.
Influence of Certain Mydriatics on Ascorbic Acid Content of Aqueous Humor. J. V. Cassady, J. M. Thompson and J. L. Pope.—p. 813.
Familial Ptosis of Eyelids Appearing in Middle Life. P. B. Cameron. —p. 818.
Functional Unilateral Mydriasis: Report of 3 Cases. J. V. M. Ross. —p. 823.
Studies in Experimental Ocular Tuberculosis: XIII. Effect of Streptomycin and Promizole® in Experimental Ocular Tuberculosis in Normal Rabbit. A. C. Woods, R. M. Wood and H. A. Naquin.—p. 834.
Id.: XIV. Failure of Aureomycin to Affect the Course of Ocular Tuberculosis. A. C. Woods, R. M. Wood and H. A. Naquin.—p. 845.
Choline Acetylase Activity in Ocular Tissues. A. deRoetth Jr.—p. 849.
Infectious Mononucleosis Complicated by Bilateral Papilloretinal Edema: Report of Case. A. Balustein and A. Caccavo.—p. 853.
Ocular Fat Embolism: Clinical and Pathologic Report. A. G. DeVoe. —p. 857.
Bilateral Anterior and Rudimentary Posterior Lenticonus. J. Fronimopoulos and T. Joannidis.—p. 864.
Pupillary Fusion Reflex. E. Marg and M. W. Morgan Jr.—p. 871.
Buried Muscle Cone Implant: I. Development of Tunneled Hemispherical Type. J. H. Allen and L. Allen.—p. 879.
Lamellar Corneal Transplantation: Preliminary Report. F. C. Stansbury. —p. 891.

Archives of Otolaryngology, Chicago

51:641-780 (May) 1950

Bone Conduction Through Auditory Ossicle Chain. P. G. MacDonald. —p. 641.
Fold and Crypt Formation in Nasopharynx: Anatomic and Clinical Study. H. Lion.—p. 655.
Threshold of Feeling in Fenestrated Ear. M. Saltzman and M. S. Ersner.—p. 667.
Forced Circling Movements (Adversive Syndrome): Correction with Dimenhydrinate ("Dramamine"). M. Schiff, W. G. Esmond and H. E. Himwich.—p. 672.
Heating of Human Maxillary Sinus by Microwaves. J. J. Ballenger and S. L. Osborne.—p. 678.
Speech Rehabilitation of Patients with Cleft Palate. E. D. Freud. —p. 685.
Cancer of Larynx Classified in Three Dimensions: Aid in Management. S. Kaplan.—p. 696.
*Tracheobronchial Aspiration Following Tonsillectomy with General Anesthesia. C. H. Steele and J. R. Anderson.—p. 699.
Selection of Patients for Fenestration Surgery. C. M. Kos and S. N. Reger.—p. 707.
Carcinoma of Ear. C. E. Towson and W. H. Shofstall.—p. 724.
Site of Lesion in Paralysis of Twelfth and/or Seventh Cranial Nerve. K. Tschiassny.—p. 739.
Origin and Treatment of Osteomas of Paranasal Sinuses. O. E. Hallberg and J. W. Begley Jr.—p. 750.

Tracheobronchial Aspiration After Tonsillectomy.—According to Steele and Anderson atelectasis and pulmonary abscess occasionally complicate tonsillectomy when the operation is done with the patient under general anesthesia. Among 129 such patients there were 125 in whom bloody secretion could be recovered, the average amount being 3.7 cc. The ideal method is that which combines proper anesthesia, proper positioning, careful operative technic and hemostasis, the use of adequate pharyngeal suction and direct laryngoscopy with tracheobronchial aspiration at the close of operation. The silk woven catheter attached to the suction tubing is atraumatic, yet stiff enough to be easily manipulated. Sizes 10 to 18 French catheters provide a range for all cases. By manipulation of the head from side to side the catheter can be caused to enter either main bronchus. The stimulating effect of the catheter on bronchial reflexes produces the so-called tussive squeeze, which clears aspirated material from the segmental branch bronchi, bringing it up to a level accessible to suction. A definite reduction in the amount of postoperative coughing and vomiting is noted in patients treated by aspiration of the tracheobronchial tree.

Archives of Surgery, Chicago

60:837-1034 (May) 1950

Carbohydrate Tolerance, Blood Ketone Levels and Nitrogen Balance After Human Trauma (Fractures). L. Sachar, W. Walker and J. Whittico.—p. 837.
Utilization of Carbohydrate in Surgical Patients: Blood Lactic Acid Levels in Preoperative and Immediate Postoperative Periods After Intravenous Administration of Dextrose. J. J. Castronuovo.—p. 845.
Tumor Formation in Atrophic Testes. J. S. Haines and H. Grabstald. —p. 857.
Unusual Case of Apparent Malingering. H. B. Shumacker Jr. and H. H. Ziperman.—p. 861.
Cetyl Dimethyl Ethyl Ammonium Bromide Chloride, New Quaternary Ammonium Agent in Surface Antisepsis. E. F. Lewison.—p. 865.
Primary Retroperitoneal Tumors: Summation of 33 Cases. H. R. Newman and B. D. Pinck.—p. 879.
Massive Cellulitis of Scalp in Persons with Diabetes. J. R. Moore, J. Gerrie and H. Elliott.—p. 897.
Neurosurgery in Young Children. H. C. Voris.—p. 906.
Surgical Anatomy of Choledochal Nerves. B. G. P. Shafiroff and J. W. Hinton.—p. 944.
Extradural Hematomas of Posterior Fossa. R. Y. Herren and W. E. Zeller.—p. 953.
Fractures of Ankle: II. Combined Experimental-Surgical and Experimental-Roentgenologic Investigations. N. Lauge-Hansen.—p. 957.
Use of Thiopental Sodium Intravenously in Presence of Hepatic Damage: Experimental Study. C. H. Walton, J. W. Uhl, W. M. Egner and H. M. Livingstone.—p. 986.
Congenital Duplication of Stomach. J. M. Miller and M. Ginsberg. —p. 995.
Pericardial Celomic Cysts: Review of Literature and Report of Case. R. A. Buyers and F. B. Emery.—p. 1002.
Anal Fistulectomy. C. J. Wagner.—p. 1006.
Duodenal Diverticula: Report of 2 Cases. J. J. Greenler and C. N. Curtis.—p. 1011.

Diseases of Chest, Chicago

17:493-616 (May) 1950

Neomycin in Experimental Tuberculosis of Guinea Pigs. A. G. Karlson, J. H. Gainer and W. H. Feldman.—p. 493.
Bed Rest, Collapse, and Streptomycin in Treatment of Pulmonary Tuberculosis: II. Toxicity Studies, and Observations on Streptomycin Sensitivity. B. W. Armstrong, W. Funk, B. J. Wilson and J. Country. —p. 503.
Clinical Appraisal of Value of Para-Aminosalicylic Acid With and Without Streptomycin in Treatment of Tuberculosis. B. P. Potter. —p. 509.
Functional Hepatic Impairment in Pulmonary Tuberculosis. R. S. Galen, D. Weiner and S. A. Hartman.—p. 524.
Intrathoracic Ganglioneuroma. J. G. Rogers and J. P. Keogh.—p. 532.
Sarcoidosis and Pregnancy. F. Aykan and N. Juskowitz.—p. 544.
Pathogenesis of Tuberculosis. C. M. Nice Jr.—p. 550.
Technique of Administering Epidural Anesthesia in Thoracic Surgery. W. W. Buckingham, A. J. Beatty, C. A. Brasher and P. Ottosen. —p. 561.
Mesothelioma of Pleura. R. E. Whitehead.—p. 569.
Technique of Bronchospirometry. G. C. Leiner and J. B. Liebler. —p. 578.
*Acute Appendicitis Occurring During Therapeutic Pneumoperitoneum. L. F. Knoepp.—p. 584.
Benign Fibroma of Pleura: Report of Case. H. R. Hawthorne and A. S. Frobese.—p. 588.

Acute Appendicitis During Therapeutic Pneumoperitoneum.—Knoepp reports 2 patients in whom appendicitis occurred in the course of a therapeutic pneumoperitoneum. Both patients were operated on and recovered. He was impressed by the rapidity with which the appendiceal infection became a general peritonitis in the face of a therapeutic pneumoperitoneum. At his hospital 184 patients have been treated with pneumoperitoneum since July 1944. The 2 reported cases were the first in which appendicitis concurred with pneumoperitoneum. The diagnosis of appendicitis in such patients would seem to justify immediate surgical intervention even in those cases where the diagnosis is doubtful.

Endocrinology, Springfield, Ill.

46:341-406 (April) 1950. **Partial Index**

Functional Significance of Testis Cholesterol in Rat: Effects of Hypophysectomy and Cryptorchidism. P. L. Perlman.—p. 341.
Factors Affecting Measurement of Proteolytic Activity of Thyroid Tissue. M. E. Kamner, A. Peranio and M. Bruger.—p. 353.
Screening Test to Indicate Opposition to Cardiovascular-Renal Effects of Desoxycorticosterone Acetate in Rat: Effect of Adrenal Cortical Extract. S. M. Friedman and C. L. Friedman.—p. 367.
Influence of Various Steroids on Oxidative Function of Rat Tissue Preparations. M. Hayano, S. Schiller and R. I. Dorfman.—p. 387.
Reactions of Thyroid Glands to Juxtathyroidal Implants of Thyrotropic Agents. A. Gorbman.—p. 397.

Georgia Medical Association Journal, Atlanta

39:185-228 (May) 1950

Medicine and Freedom. E. E. Irons.—p. 185.
The Welfare State Versus Welfare of the State. E. Callaway. —p. 191.
Carotid Sinus Syndrome. C. R. Arp, H. M. Davison and J. S. Atwater.—p. 196.
Roentgen Therapy for Bursitis of Shoulder. D. Robinson.—p. 205.
Diagnostic and Therapeutic Block for Treatment of Pain. C. M. Brown.—p. 209.

Journal of Allergy, St. Louis

21:181-272 (May) 1950. **Partial Index**

Atopic Dermatitis: I. Experimental Clinical Study of Role of Inhalant Allergens. L. Tuft, H. S. Tuft and V. M. Heck.—p. 181.
Asthma with Sinus Disease: Comparison of Radical Sinus Surgery and Conservative Treatment. J. L. Guerrant, A. McCausland and O. Swineford Jr.—p. 187.
Asthma Complicated by Recurrent Spontaneous Pneumothorax. J. R. Wiseman, B. T. Brown and A. G. Gandia.—p. 199.
*Sudden Death Due to Allergy Tests. M. C. Harris and N. Shure.—p. 208.
Effect of Development of Eczematous Sensitization to Drug on Pharmacologic Properties of Drug. A. Rostenberg Jr., J. H. Last and A. A. Rodriguez.—p. 217.
Factors Influencing Reagin Formation in Experimental Human Sensitization to Ascaris Lumbricoides Antigen: IV. Influence of Previous Sensitization on Rate of Sensitization. E. W. Kailin, E. A. Rossbach and M. Walzer.—p. 225.
Ventilatory Tests in Bronchial Asthma: Evaluation of Vital Capacity and Maximum Breathing Capacity. E. A. Gaensler.—p. 232.

Sudden Death Due to Allergy Tests.—Harris and Shure report a woman, aged 25, with asthma and hay fever who had received injections of house dust and pollens from the age of 5 until 18 with satisfactory results. She was symptom-free and did not require treatment for 6 years thereafter. In the year prior to her admission to the clinic, there was a recurrence of stuffiness of the nose and of wheezing dyspnea. Physical examination at this time led to a provisional diagnosis of allergic rhinitis and bronchial asthma. Intradermal tests were performed with routine testing strengths of local pollen extracts. Mild reactions, 1 and 2 plus, were obtained to various grasses. An iodide mixture was prescribed and the patient was asked to return the following week for further skin tests. At this visit skin testing was resumed with extracts of miscellaneous environmental substances. Within one minute after these intradermal tests had been completed, the patient developed severe dyspnea. She rapidly became moribund despite repeated injections of epinephrine. As a last resort, a tracheotomy was performed. She expired within 10 minutes after the onset of the initial dyspnea despite the administration of oxygen through the tracheotomy opening, artificial respiration, and cardiac and respiratory stimulation, including epinephrine intracardially. Necropsy revealed findings typical of a fatal anaphylactic reaction. Allergy tests made with the patient's serum on a nonallergic subject and passive transfer and dilution studies indict the cottonseed allergen as the cause of the fatal reaction. Cottonseed has been recognized as a potent allergen, but the authors are aware of only 2 deaths prior to this one. The cottonseed extract used in testing the patient was of routine testing strength. The vial of extract from which the fatal dose was removed had been used for testing other patients with no constitutional reactions. The author advocates preceding intradermal tests with scratch tests.

Journal of Aviation Medicine, St. Paul

21:77-170 (April) 1950

Immediate and Accumulative Effect on Psychomotor Performance of Exposure to Hypoxia, High Altitude and Hyperventilation. J. Scow, L. R. Krasmo and A. C. Ivy.—p. 79.
High Altitude-High Velocity Flying with Special Reference to Human Factors: I. Outline of Human Problems. A. P. Webster.—p. 82.
Controlled Study of Effects upon Brains of Guinea Pigs of Ultrasonic Waves Generated by Turbo-Jet Engines. H. H. Wilcox and W. F. Windle.—p. 85.
Studies on Airsickness. B. A. Strickland Jr., G. L. Hahan and H. Adler.—p. 90.
Biochemistry in Relation to Aviation Medicine: Survey of Literature. G. M. Everhart.—p. 98.
Audiological Aspects of Aircraft Noise. W. J. Pothoven.—p. 140.
Electro-Myography as Test for Pilot Aspirants. A. Lunderwold. —p. 147.
Aero-Otitis Media in Infants. R. L. Fruin.—p. 150.
Role of Adrenal Glands in Utilization of Oxygen. M. A. Goldzieher. —p. 153.
Physical Fitness. P. C. Platt.—p. 160.

Journal of Bacteriology, Baltimore

59:449-602 (April) 1950. **Partial Index**

Effect of Monochromatic Ultraviolet Radiation on Infectivity and Hemagglutinating Ability of Influenza Virus Type A Strain PR-8. I. Tamm and D. J. Fluke.—p. 449.
Antisporulation Factors in Complex Organic Media: I. Growth and Sporulation Studies on Bacillus Larvae. J. W. Foster, W. A. Hardwick and B. Guirard.—p. 463.
Yeasts from Hawaiian Fruit Flies: Their Identification and Ability to Produce Riboflavin. L. R. Hedrick and G. C. Burke.—p. 481.
Acetic Acid Oxidation by Escherichia Coli and Aerobacter Aerogenes. S. J. Ajl.—p. 499.
Influence of Certain Salts, Amino Acids, Sugars and Proteins on Stability of Rickettsiae. M. R. Bovarnick, J. C. Miller and J. C. Snyder. —p. 509.
Production of Streptocin by Different Strains of Streptomyces Griseus. A. B. Kupferberg, H. Styles, H. O. Singher and S. A. Waksman. —p. 523.
Immunization with Heat-Killed Mycobacterium Paratuberculosis in Mineral Oil: II. B. Sigurdsson and A. G. Tryggvadóttir.—p. 541.
Comparative Study of Known Food-Poisoning Staphylococci and Related Varieties. J. B. Evans and C. F. Niven Jr.—p. 545.
Chromatin Staining of Bacteria During Bacteriophage Infection. S. E. Luria and M. L. Human.—p. 551.
Electron and Light Microscopic Studies of Bacterial Nuclei. S. Mudd and A. G. Smith.—p. 561.

Journal of Clin. Endocrinology, Springfield, Ill.

10:479-582 (May) 1950

Urinary Corticosteroid Values of Children as Determined Chemically. N. B. King and H. L. Mason.—p. 479.
Failure of Hypophyseal Growth Hormone to Produce Nitrogen Storage in a Girl with Hypophyseal Dwarfism. L. L. Bennett, H. Weinberger, R. Escamilla and others.—p. 492.
Quantitative Determination of Urinary Pregnanediol in Pregnant Women: Influence of Method upon Results. O. W. Smith.—p. 496.
Basal Temperature Studies in Aged Female; Influence of Estrogen, Progesterone and Androgen. D. T. Magallon and W. H. Masters. —p. 511.
Alterations in Serum Iodine Fractions Induced by Administration of Inorganic Iodide in Massive Dosage. T. S. Danowski, S. Y. Johnston and J. H. Greenman.—p. 519.
Serum Iodine Fractions in Subjects Receiving Potassium Iodide in Small Dosage. T. S. Danowski, F. Mateer, F. A. Weigand and others.—p. 532.
Panhypopituitarism: Case Report Correlating Clinical and Pathologic Findings. D. G. McKay, C. H. Burnett and B. A. Burrows. —p. 540.
Hyperglycemic Factor Extracted from Pancreas. I. J. Pincus.—p. 556.

Journal of Insurance Medicine, Louisville, Ky.

5:1-64 (March-April-May) 1950. **Partial Index**

Hypertensive Sequelae of Toxemias of Pregnancy. L. C. Chesley.—p. 11.
Gonorrhea in the Female. A. G. King.—p. 15.
Prognosis in Myasthenia Gravis. S. J. Weisman.—p. 17.
Problem of Low Back Pain. G. S. Phalen.—p. 20.
Chronic Brucellosis. R. J. Ralston.—p. 24.
Routine Examination of Genito-Urinary Tract. R. Roth, A. F. Kaminsky and E. Hess.—p. 27.
*Lymphogranuloma Venereum and Granuloma Inguinale. B. A. Kornblith.—p. 30.

Lymphogranuloma Venereum and Granuloma Inguinale.—Kornblith stresses that lymphogranuloma venereum and granuloma inguinale are separate and distinct clinical entities. Lymphogranuloma venereum now includes a number of conditions previously described as lymphogranuloma inguinale, lymphopathia venereum, climatic bubo, esthiomene, inflammatory rectal stricture, perianal condyloma, rectovaginal fistula, stenosis of the vagina and anorectal syphiloma. These different entities result from lymphatic involvement of the pelvic structures by this disease which is caused by a filtrable virus. The diagnosis is based on the clinical findings which are substantiated by a positive Frei test, which consists of intracutaneous injection of 0.1 cc. of a prepared antigen (chick embryo lygranum). Granuloma inguinale, termed also granuloma venereum, is produced by Donovan bodies. This disease manifests itself for the most part on the skin near or on the genitals and inguinal regions. It may occur in other parts of the body. No rectal strictures are present in this disease. The clinical appearance is that of a chronic granulomatous process involving the groin and spreading in the genital area with little pain. There is little involvement of the lymph nodes. The diagnosis is ascertained by the finding of Donovan bodies in the monocytes of tissue scrapings. In over half of the cases of lymphogranuloma venereum or granuloma inguinale there exists an associated second venereal disease. Treatment of lymphogranuloma venereum and granuloma inguinale consists of the adequate use of streptomycin, aureomycin and chloramphenicol. Occasionally surgery becomes necessary after the activity of the diseases has been counteracted by adequate antibiotic therapy.

Nebraska State Medical Journal, Lincoln

35:97-136 (April) 1950

Laboratory and Clinical Trials of Five Local Anesthetics. A. R. McIntyre, L. W. Lee, J. A. Rasmussen and others.—p. 100.
Aureomycin in Cutaneous Therapy. G. F. Pinne.—p. 104.
Gaucher's Disease. J. R. Schenken.—p. 106.

Public Health Reports, Washington, D. C.

65:555-582 (April 28) 1950

Statistical Studies of Heart Disease: VI. Age at Onset of Heart and Other Cardiovascular-Renal Diseases. T. D. Woolsey.—p. 555.

65:583-618 (May 5) 1950

Biological Assay of Lots of Histoplasmin and Selection of New Working Lot. L. W. Shaw, A. Howell Jr. and E. S. Weiss.—p. 583.

65:619-650 (May 12) 1950

Relationship of Coliform Bacteria to Gas Production in Media Containing Lactose. C. W. Chambers.—p. 619.
Experimental Histoplasmosis in Dog: Nonfatal Case. R. W. Menges, M. L. Furcolow and J. S. Rube.—p. 628.

65:651-682 (May 19) 1950

*Method of Home Care for Prolonged Illness. S. Shindell.—p. 651.
Ideological Barriers to Effective Teaching by Health Workers. E. J. Anderson.—p. 661.
Rapid Measurement of Carbohydrate in Blood: Preliminary Report. W. F. Durham, W. L. Bloom, G. T. Lewis and E. E. Mandel.—p. 670.

Home Care for Prolonged Illness.—Shindell deals with experiences at Montefiore Hospital in the Bronx, where home care has been arranged for a total of 261 patients in the last two years. The Public Health Service cooperated in setting up and observing the program. Hospital care is becoming prohibitive for cases of prolonged illness, and the home care plan seems a partial solution of the problem of how to reduce the costs of chronic illness. Many patients with long term illnesses require the facilities of the hospital for only a small part of the time spent in the hospital bed. When the home care program operates effectively, the personalized care these patients receive is superior to hospital care. About 70 per cent of those with long illnesses can best be cared for in the home, provided there is adequate supervision and assistance. Cost of caring for a patient at home is only one third to one fifth that of hospital care. The purpose of this report is in part to dispel the impression that the method is simple in its execution. Home care of chronically ill patients must be considered as an extension of hospital care, calling for closely integrated work by physicians, medical social workers, nurses and occupational and physical therapists. Adequate facilities must exist in the home, and a high degree of cooperation must be achieved between the family of the patient and the hospital personnel.

Rhode Island Medical Journal, Providence

33:165-220 (April) 1950

Treatment of Peptic Ulcer. F. Glenn, C. Forkner, S. W. Moore and T. P. Almy.—p. 179.
Cardiovascular Syphilis (Report from the Cardiovascular Division of Syphilis Clinic, Rhode Island Hospital Outpatient Department). C. B. Leech.—p. 186.

Yale Journal of Biology and Medicine, New Haven

22:387-466 (May) 1950

Origin of the Word Protein. H. B. Vickery.—p. 387.
Studies of Electrophoretic Serum Protein Patterns in Subjects Treated with Pituitary-Adrenal Cortical Hormones, Nitrogen Mustard or X-Radiation. K. Frieden and A. White.—p. 395.
Induction of Lupus Erythematosus ("L. E") Cell in Vitro in Peripheral Blood. R. N. Hamburger.—p. 407.
Transducers for Multichannel Studies in Neuropharmacology. E. L. McCawley, J. A. Riley and A. Mauro.—p. 411.
Relation of Amino Acids to Trypanocidal Activity of Parascorbic Acid. B. A. Rubin.—p. 423.
Diarrhea in Otherwise Healthy Infant. A. S. Brackett.—p. 429.
Developments in Electroencephalography: Basal and Temporal Regions. P. D. MacLean.—p. 437.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted.
Single case reports and trials of new drugs are usually omitted.

British Journal of Radiology, London

23:261-316 (May) 1950. **Partial Index**

*Association of Cancer of Gastric Cardia with Partial Thoracic Stomach, Short Oesophagus and Peptic Ulceration. D. W. Smithers.—p. 261.
Carcinoma in Herniated Gastric Cardia Associated with Short Oesophagus. J. Dawson and H. G. H. Richards.—p. 270.
Generalised Lipomatosis Involving Bone: Report of Case. M. H. Fainsinger and L. C. Harris.—p. 274.
Mechanical and Physical Problems of Angiocardiography. T. H. Hills. —p. 279.
Calculation of Energy Deposition by Fast Neutrons in Soft Tissue. J. H. Tait.—p. 282.

Cancer of Cardia with Partial Thoracic Stomach.—Smithers reviews evidence in support of the theory that both congenital shortening of the esophagus and acquired shortening due to cicatrization following ulceration are comparatively rare and that the majority of cases diagnosed as short esophagus radiologically are primarily cases of hiatus insufficiency associated with spasm of the longitudinal muscle fibers of the esophagus. Herniation of the cardia into the mediastinum interferes with the valve control and allows acid to flow into the esophagus. Esophagitis and peptic ulceration may follow the regurgitation. Shortening of the esophagus, due to contraction, may result from reflex stimulation due to irritation from some abnormality in the esophagus or upper part of the abdomen, and may either pull part of the stomach through a lax hiatus or may follow herniation, due to some other cause, when irritation due to regurgitation of gastric contents causes the contraction which then takes up the slack. In some cases the shortening may become permanent due to fibrosis and fixation, but the comparative rarity of postmortem reports of such cases and the way in which the herniation can often be reduced at operation suggest that this does not usually occur. The development of cancer has been noted in a few of these patients, 4 new instances being reported here. Three possible reasons for the association are discussed, firstly, that it may be a chance occurrence, secondly, that the esophagitis that results may predispose to the development of cancer and, thirdly, that the carcinoma acts as an irritative focus causing contraction of the esophagus and at the same time increases intra-abdominal pressure, thus helping to dilate the esophageal hiatus and predispose to herniation.

British Medical Journal, London

1:973-1020 (April 29) 1950

*Carcinoma of Stomach. H. C. Edwards.—p. 973.
Necropsy Findings in Case of Q Fever in Britain. J. W. Whittick. —p. 979.
*Placental Metastases in Malignant Disease Complicated by Pregnancy with Report of 2 Cases. S. Bender.—p. 980.
Carcinoma of Islets of Langerhans with Hypoglycaemia. B. F. Brearley and J. W. Laws.—p. 982.
Aureomycin in Brucellosis. E. W. Lindeck.—p. 985.
Brachial Neuralgia. W. M. Philip.—p. 986.
Complete Excision of Parotid Gland with Preservation of Facial Nerve. H. A. Kidd.—p. 989.
Scarlet Fever and Tonsillitis in Relation to Acute Rheumatism. T. C. Macdonald.—p. 992.

Carcinoma of Stomach.—Edwards believes that the gloomy implications engendered by mass statistics on cancer of the stomach should not be accepted without challenge, because the condition is as amenable to surgical cure as carcinoma of the breast in a comparable stage of the disease. The natural history of cancer of the stomach is not, on the average, as short as is sometimes believed. The growth may be a localized lesion for a considerable time. It is probable that in some types of carcinoma there are diffuse precancerous changes in the mucosa which may themselves be responsible for the symptoms. Edwards stresses the importance of the history in diagnosis, pointing out that it outweighs in significance all ancillary methods, including roentgenograms. Roentgenologic examination may itself be responsible for delay in the diagnosis. It was the author's experience that by the time the radiologist was in a position to say that an ulcer of the lesser curvature or of the prepyloric region was malignant beyond doubt the growth had passed the stage in which there was a probability of cure. Though the growth may be operable in the sense that all disease apparent to the naked eye may be eradicable, the prognosis is poor and may be compared to that in late cases of carcinoma of the breast in which there is involvement of the overlying skin and enlargement of the axillary nodes. The radiologist is often made to carry too heavy a responsibility—more than is justified by the ability of radiography to diagnose cancer at an early stage. Of the ancillary diagnostic methods other than radiology none is consistently reliable. The scope of surgery, the extent of the radical operation and the nature of palliative operations are reviewed. Ulcers in the pyloric antrum should always be regarded as actually or potentially malignant and should be operated on. It is impossible at an early stage to distinguish between simple and malignant ulcers developing in this situation. The validity of routine total gastrectomy for growths of the distal portion of the stomach is not proved. A portion of the stomach should be left so that the cardia remains intact. A laparotomy should be enjoined in the presence of a suggestive history even when other investigations have yielded negative or equivocal results.

Placental Metastases in Malignant Disease.—Bender has encountered 6 instances of maternal malignant disease in association with pregnancy. The placenta and cord in 1 patient were macroscopically normal and were not examined microscopically. Serial sections were studied in the others. In addition, when the fetus was aborted or stillborn necropsy was performed and the organs were studied microscopically. The authors describe 2 cases, which make the eighth and ninth cases of metastasis of a maternal tumor to the products of gestation to be reported. Secondary deposits were found in the placenta in both cases, but the umbilical cords and the babies were not affected. Both patients died, one eight hours and the other 10 weeks after the delivery. The prognosis for the mother is poor if metastases are present in the placenta in the absence of demonstrable secondary growths elsewhere. A plea is made for the routine histologic examination of the products of gestation in all cases of maternal malignant disease complicated by pregnancy. In this way the frequency of placental metastases may be more accurately estimated and the prognosis for the mother may thereby be revealed.

Edinburgh Medical Journal

57:129-144 and 1-46 (March) 1950

*Observations on Liver Function in Heart Failure. A. W. Branwood. —p. 129.

SYMPOSIUM ON HAEMODYNAMICS IN PREGNANCY

Cardiac Output in Pregnancy. H. F. H. Hamilton.—p. 1.
Limb Volumes in Normal and Toxaemic Pregnancy. R. White.—p. 10.
Blood Volume in Pregnancy. R. White.—p. 14.
Peripheral Circulation in Pregnancy. C. C. Burt.—p. 18.
Haemodynamics in Pregnancy. R. J. Kellar.—p. 27.

Liver Function in Heart Failure.—Branwood analyzed the clinical features of patients with heart failure in an effort to determine the part played by chronic venous congestion of the liver in the production of their symptoms. He discusses the methods of palpation and percussion to be used in order to ascertain the enlargement of the liver and says that in 456 cases of congestive cardiac failure the liver was found to be enlarged in every patient. If the enlargement of the liver occurs rapidly the organ becomes tender owing to the sudden stretching of the capsule; 212 patients complained of pain in the right part of the hypochondrium. Patients are frequently

encountered in whom the liver is enlarged but in whom there is little or no obvious venous distention or increase in venous pressure. In this series the liver remained enlarged in 22.5 per cent after their apparent recovery. Latent jaundice is invariably present in patients with congestive cardiac failure. Clinical jaundice is often seen, but it may be masked by the cyanosis. The presence of clinical jaundice in patients with congestive cardiac failure usually indicates a bad prognosis. In this series 126 out of 456 patients with congestive failure had clinical jaundice and of these 81 died. Ascites is common in congestive failure; it was present in 360 of the 456 patients. Urobilinogen is present in excess in the urine of patients with cardiac failure. It diminishes when the failure is treated. Eighty-six patients in this series complained that they had poor appetite and found it impossible to eat large meals several weeks before the onset of their heart failure. Twelve patients when questioned admitted having similar symptoms. These symptoms are presumably caused by chronic engorgement of the stomach resulting from venous stasis in the congested liver. Flatulence is another common feature in these patients. The author reviews experiences with liver function tests and states the belief that if any of the tests shows a decidedly positive result, this indicates a bad prognosis. Cardiac cirrhosis or hepatic fibrosis of heart disease cannot be diagnosed with certainty.

Irish Journal of Medical Science, Dublin

203:209-256 (May) 1950. **Partial Index**

Aspects of Muscle Physiology. E. J. Conway.—p. 209.
Strains of Ankle Joint. C. Somerville-Large.—p. 225.
*Bilateral Alveolar Lung Carcinoma, Associated with Injection of Thorotrast. L. Abrahamson, M. H. O'Connor and M. L. Abrahamson. —p. 229.
Post-Cricoid Cancer. C. K. Byrnes.—p. 236.

Bilateral Lung Carcinoma After Use of Thorotrast.—Abrahamson and associates present the case of a woman who developed pulmonary tumor with many exceptional features 16 years after she had been injected with 75 cc. of the radioactive substance thorotrast. In 1932 she had attended the outpatients' department, and because of a splenic enlargement was given thorotrast by a medical officer, who was investigating the efficacy of this substance in outlining the liver and spleen. The dose administered was 10 cc. intravenously on the first day, 15 cc. on the next day and 25 cc. on each of the following days to a total of 75 cc. The patient's liver and spleen showed the continued presence of thorotrast till death. At postmortem spleen and liver were still radioactive from the presence of thorium. The lungs were not radioactive but their examination revealed a primary alveolar tumor of mucus-secreting type and of malignant behavior, with a unique distribution throughout both lungs. The authors discuss the possible origin of the tumor from the injections of thorotrast and its primary rather than metastatic nature. The whole alveolar area of both lungs had undergone a total metaplasia and then a hyperplasia in a manner and to a degree that has never been described as associated with a metastasis. The only comparable tumors that come to mind are those of the hemopoietic tissue or the generalized primary tumor known as polyposis coli.

Journal of Neurol., Neurosurg. & Psychiatry, London

13:89-158 (May) 1950

Degeneration of Peripheral Nerve Fibres. E. Gutmann and J. Holubář. —p. 89.
*Uraemic and Trophic Deaths Following Leucotomy: Neuro-Anatomical Findings. T. McLardy.—p. 106.
Hemiballismus: Aetiology and Surgical Treatment. R. Meyers, D. B. Sweeney and J. T. Schwidde.—p. 115.
Simplified Suboccipital Technique for Trigeminal, Acoustic, or Glossopharyngeal Rhizotomy. E. Walker.—p. 127.
Hereditary Spastic Paraplegia with Amyotrophy and Pes Cavus. H. G. Garland and C. E. Astley.—p. 130.
Hereditary Spastic Paraplegia. E. R. Bickerstaff.—p. 134.
Methods of Impregnating Neurofibrillar Substance on Slides After Imbedding. P. Mihálik.—p. 146.
Case Report: Mental State During Recovery After Heart Arrest During Anaesthesia. H. Turner.—p. 153.

Uremic and Trophic Deaths Following Leukotomy.—McLardy, in an earlier report, deduced from a study of the brains and clinical records of 101 leukotomy cases that probably as high a proportion of "the leukotomized population" dies a delayed operative death within five months of the operation as from a hemorrhage within two weeks of the operation. At that time he had not decided what lesions might be responsible. A more precise anatomic analysis has now been carried out. The brain material and clinical records of 122 leukotomy cases have been collected from some 40 British hospitals, and from among this material 22 patients have been selected who died within 6 months of their leukotomy. Analysis of the causes of death revealed two distinct groups: Group 1, dying predominantly from uremia in the third postoperative week, and group 2, dying predominantly from trophic deterioration (marasmus with trophic skin lesions) between two and five months after the operation. In the latter group blisters or bullae almost always appeared on the extremities between the fourth and sixth postoperative weeks. Postmortem analysis of the lesions in the frontal lobes of these 22 patients revealed a striking association of death from uremia with bilateral damage to the posterior (nongranular) orbital cortex and of death from trophic deterioration with bilateral cutting of the region of the subcallosal fasciculus at the level of the head of the caudate nucleus. The orbital cortex concerned in the uremic deaths appeared to be posterior area 47, not area 13. Microscopic evidence of nutritional deficiency was not conspicuous among the cases of trophic deterioration. From evidence supplied by these and other relevant cases, it is deduced that connections between the caudate nucleus and Brodmann's (nongranular) cortical areas 8 and 6 (including their mesial extension toward the corpus callosum), via the rostral parts of the subcallosal fasciculus, may be the structures whose damage determined the fatal trophic deterioration. The author emphasizes the serious danger of delayed operative death from the use of blind leukotomy technics, including the "deep" transorbital cut.

Journal of Physiology, Cambridge

111:1-214 (April 15) 1950. **Partial Index**

Responses of Blood Vessels of Muscles with Special Reference to Their Central Control. R. J. S. McDowall.—p. 1.
Responses of Heart Rate and Systolic Blood Pressure to Series of Sympathomimetic Amines in Unanaesthetized, Atropinized Bitch. M. F. Lockett.—p. 19.
Immediate and Delayed Effects of Diisopropylfluorophosphate Injected into Supraoptic Nuclei of Dogs. H. N. Duke, M. Pickford and J. A. Watt.—p. 81.
Synthesis of Acetylcholine in Wall of Digestive Tract. W. Feldberg and R. C. Y. Lin.—p. 96.
Inorganic Components of Gastric Secretion. R. B. Fisher and J. N. Hunt.—p. 138.
Accuracy of Meyerstein Haematocrit. D. M. Jackson and M. E. Nutt. —p. 150.
Response of Rabbit's Endometrium to Uterine Implants of Progesterone and Other Steroids. E. O. Höhn and J. M. Robson.—p. 174.

Lancet, London

1:841-888 (May 6) 1950

*Streptomycin in Acute Miliary Tuberculosis: Report to the Medical Research Council.—p. 841.
*Surgery in Parkinson's Disease: Complete Section of Lateral Column of Spinal Cord for Tremor. L. C. Oliver.—p. 847.
Further Observations on Potency of Oestrogens: Clinical Assessment. P. M. F. Bishop, N. A. Richards and D. J. N. Smith.—p. 848.
Activity of Further Synthetic Oestrogens Determined by Experiments on Rats. G. L. M. Harmer and W. A. Broom.—p. 850.
Myxoedema from Resorcinol Ointment Applied to Leg Ulcers. G. M. Bull and R. Fraser.—p. 851.
Effect of Resorcinol on Thyroid Uptake of I^{131} in Rats. I. Doniach and R. Fraser.—p. 855.
Serological Diagnosis of Herpes Simplex Infections. M. E. Hayward. —p. 856.
Typhoid Fever Treated with Chloramphenicol: Development of Carrier State. A. D. M. Douglas.—p. 858.

Streptomycin in Acute Miliary Tuberculosis.—According to the report of the Medical Research Council a trial of streptomycin in acute miliary tuberculosis was begun by a trials committee of the council early in 1947. This report analyzes the records of the patients admitted for treatment under the scheme between March 22 and Sept. 30, 1947. There were 25 patients. The 14 survivors have been followed for two years. Apart from the 3 patients who died in less than a week all but 1 showed clinical response to treatment. Uninterrupted recovery took place in 9; 1 recovered from miliary disease, but with residual pulmonary tuberculosis; 8 developed meningitis, and 4 of these died; 4 died without meningitis. The miliary lesions in the lungs cleared in 19 of the 21 patients who survived more than two months. The prognosis was much worse in the

patients most acutely ill at the start of treatment than in the others: 10 of the 11 deaths and 7 of the 8 cases of meningitis occurred among the 16 patients with temperatures of 101 F. or over at the start of treatment.

Section of Lateral Column to Counteract Tremor of Parkinson's Disease.—Oliver described previously the effects of a 5 mm. cut into the posterior part of the lateral column. In an attempt to improve further the results he increased the extent of the incision in the cord to include the whole of the lateral column. In this new operation the lateral column is divided on the side of the tremor. The immediate effects of the operation are total absence of tremor, hemiplegia on the same side and loss of sensation to pain and temperature on the opposite side. Later a little tremor is to be found at times of mental stress, and the hemiplegia usually recovers almost completely but the hemianalgesia and hemithermanesthesia are permanent. Patients selected for complete division of the lateral column should have the disease confined strictly to one side. A patient with tremor on one side is not necessarily suffering from unilateral disease for there may be mental changes, a bilateral masking of the face and some rigidity of the opposite side to reveal that both sides are affected. The radical operation, the subject of this article, is not advised if there is the slightest evidence of bilateral disease, partly because it is unjustifiable to leave a patient with bilateral analgesia. A history from relations should reveal no unfavorable mental changes. There should be masking of one side of the face only. When the patient walks, the unaffected arm should swing freely and there should be no suspicion of disability or rigidity on this side. If the tremor is presenting symptom, the surgeon must discover what part it plays in the patient's life as well as its importance in relation to the other manifestations of the disease.

Tubercle, London

31:73-96 (April) 1950

Investigation into Factors Contributing to Relapse in Cases of Pulmonary Tuberculosis Treated by Unilateral Artificial Pneumothorax. G. P. Maher-Loughnan.—p. 74.
Fluorescence Microscopy. M. H. Jennison and A. F. Morgan.—p. 84.

31:97-120 (May) 1950

Investigation into Factors Contributing to Relapse in Cases of Pulmonary Tuberculosis Treated by Unilateral Artificial Pneumothorax. G. P. Maher-Loughnan.—p. 98.
Tuberculosis and Employment. W. D. Gray.—p. 108.

Archivio Italiano di Chirurgia, Bologna

72:209-282 (No. 4) 1949. **Partial Index**

*Symptoms and Operability of Cancer of Lung. G. Marcozzi.—p. 209.

Symptoms and Operability of Cancer of Lung.—Marcozzi reports on 100 patients with primary cancer of the lung. Forty-three of these were inoperable and exploratory thoracotomy in 28 demonstrated inadvisability of a radical operation; 27 patients had a radical operation, and 2 patients refused operation. The early clinical symptoms were those of bronchopulmonary disease, either primary or recurrent, followed by chest pain or shoulder pain of a neuralgic or arthritic type. A correct diagnosis of cancer of the lung from appearance of the first symptoms was made in 18 cases. In the remaining patients the diagnosis was rheumatic neuralgia in 23, tuberculosis in 18, bronchopneumonia in 16, abscess of the lung in 12, echynococcic cysts of the lung in 10 and pleuritis and atelectasis in 6. The rate of inoperability was high for patients who complained of hemithoracic or shoulder pain as the first symptom, whereas the rate of operability for patients with cough as the earliest symptom was high. Early appearance of subacute or acute chest pain as the first symptom of cancer of the lung indicates early involvement of the pleura. Indefinite pain irradiating to the anterior and posterior regions of the thorax suggests invasion of the mediastinum by a peripheral pulmonary tumor, while cough, hematemesis, expectoration of tumor tissue and irregular fever indicate cancer of the central zones of the lung. The rate of operability in patients with the aforementioned symptoms is high provided the time between appearance of symptoms and performance of a radical operation does not exceed five and a half months. The appearance of any of the aforementioned symptoms in patients over 40 calls for diagnostic studies by roentgen and stratigraphic examinations, bronchoscopy, bronchography and examination of the sputum for cancer cells.

Chirurg, Heidelberg

21:65-128 (Feb.) 1950. **Partial Index**

Intravenous Meperidine-Evipan Sodium (Barbital Derivative) Narcosis. A. Hofmann.—p. 65.
Experiences with Preserved Blood in 2500 Transfusions. E. Domanig.—p. 68.
Pathogenesis of Local Bone Necroses. M. Mennenga.—p. 71.
*Therapy of Air Embolism. B. Hummel.—p. 73.
*Efficacy of Protective Effect of Mouth Mask. R. Schneider.—p. 74.
Paramedian Extraperitoneal Incision and Its Applicability in Urology. W. Rieder.—p. 78.
Plastic Surgery on Stumps. W. Block.—p. 82.
Methods for Surgical Treatment of Habitual Luxation of Shoulder. E. Hellenthal.—p. 87.

Therapy of Air Embolism.—Referring to earlier reports by Weese and by Lembcke, Hummel says that he too succeeded in counteracting complete respiratory and cardiac arrest after air embolism by puncture and aspiration of the right auricle with a 2 mm. caliber needle. His patient had an arteriovenous aneurysm of the innominate artery as the result of a shell injury. In the course of dissection the wall was torn; this was immediately followed by massive air embolism, which caused respiratory arrest, complete stoppage of pulsation and cyanosis. Prompt puncture and aspiration of the right auricle immediately restored respiration and pulsation. No blood emerged from the needle in the auricle, but several bubbles escaped. The needle was withdrawn from the auricle after respiration and pulsation had been restored, and at first the condition remained unchanged. Later, when manual pressure on the damaged site was relaxed a new air embolism resulted, but renewed puncture proved ineffective. Postmortem examination revealed that the second puncture had failed to reach the auricle. The necropsy proved the presence of air embolism and showed that the first puncture had actually reached the auricle, whereas the second one had not.

Efficacy of Mouth Mask.—Schneider describes studies on the effectiveness of mouth masks in insuring asepsis in surgical operations. Persons spoke for several minutes and coughed a number of times while wearing surgical masks. The aim was to ascertain the number of micro-organisms that escaped from mouth and nose through the masks and onto agar plates 3 cm. or 40 cm. removed from the mouth. His studies revealed that the mask does not insure complete protection against the emergence of micro-organisms from the mouth, but the number of micro-organisms that escape is small. There was no difference in bacterial count on the agar plates whether the nose was covered or open, provided the person was healthy. Diseases of the oral or nasal cavities cause a considerable increase in the bacterial flora, so that more micro-organisms emerge during coughing and talking. Loud speaking causes the passage of more micro-organisms through the mask than speaking in a low voice. A poorly fitting mouth mask does not prevent dispersion of organisms that emerge from the mouth. The colonies that grew on the agar plates included hemolytic staphylococci and streptococci. These were detected most frequently in persons with infections of the air and food pasages; they account for 9 per cent and 2 per cent, respectively, of the colony growth on the plates held at a distance of 3 cm. and 40 cm.

Journal de Médecine de Lyon

31:231-276 (March 20) 1950. **Partial Index**

*Experimental Reproduction of Vascular Lesions with Desoxycorticosterone. P. Ravault, P. Guinet and J. Traeger.—p. 231.
*Contribution to Study of Treatment and of Prognosis of Tuberculous Meningitis: Statistics of Streptomycin Department of Hospitals of Lyon. A. Gonin, P. Galy, M. Exbrayat and others.—p. 237.
Blood Phosphatase During Twin Pregnancy: Pathogenesis and Treatment. M. Dumont and M. Poulet.—p. 253.

Experimental Vascular Lesions Produced with Desoxycorticosterone.—Ravault and co-workers injected desoxycorticosterone in 50 mg. crystalline suspension into two series of rats, each of which consisted of 3 male and 3 female animals. One animal in each series served as control and did not receive injections. The injections were made in the thigh every two weeks for a period of five months, at the end of which the animals were killed. Microscopic examination of the mesenteric vessels, the kidneys and the myocardium demonstrated a definite

effect on the connective tissue and particularly on the arterial coats. Endarteritis proliferans, hyaline necrosis of the media and fibroblastic and collagen hyperplasia of the adventitia were observed. The lesions varied in various organs. Localized lesions of the periarteritis nodosa type were predominant in the intestines. The lesions in the kidneys showed a striking analogy to those of nephroangiosclerosis. The myocardium displayed islets of interstitial sclerosis. These observations confirm strictly those of Selye. It is too early to assert that these experimental lesions may have their counterparts at the clinical level.

Streptomycin in Tuberculous Meningitis.—Gonin and associates treated with streptomycin 62 patients (20 men, 17 women and 25 children) with tuberculous meningitis. Twenty-nine patients (8 women, 12 men and 9 children) died. Cure was obtained in 23 patients (4 men, 6 women and 13 children). Stabilization resulted in 7 patients (3 men, 2 women and 2 children). The remaining 3 patients were lost to follow-up. The prognosis is more favorable in children than in adults, and the greater mortality rate in men as compared to women may be accounted for by a greater incidence of meningitis secondary to progressive visceral tuberculosis. Hyperactive forms of meningoencephalitis were not exceptional. The determination of the chloride and sugar level in the cerebrospinal fluid seemed to be of equal value in diagnosis and in control of the course of the disease. Inoculation and cultures were frequently negative in meningitis with a definite etiologic basis. Treatment with large doses of streptomycin, 3 to 4 Gm. daily in adults and 2 to 3 Gm. daily in children, was given by the intramuscular route for two weeks. Intraspinal injections were given for twenty-five to thirty days, with a daily dose of 100 to 150 mg. of the drug in adults. This route must be employed in every case in which its use is not associated with risk and in which it does not induce intense meningeal reaction. General treatment with streptomycin should be continued with doses of 1.50 to 2 Gm. daily for one month and with doses of 1 to 1.50 Gm. for several months afterward. Results were best in patients treated for eighteen months. Six to seven months of treatment are required to obtain a stabilization. Recurrence of activity at that time is not rare. The occasionally favorable course of these recurrences and of recurrences long after treatment had been discontinued is proof that resistance of organisms to streptomycin is not the cause of the therapeutic failure. Intracranial hypertension, meningeal block and cerebral involvement occurred in 7 instances in the course of treatment, particularly during the first months. The early occurrence of this hypertension is a contraindication to surgical intervention, which may be more effective in late forms. Necropsies were performed in 15 cases and revealed the elective or strongly predominant involvement of the region of the optic chiasm and of the tuber. The dense fibrocaseous meningeal adhesions explain the recurrences and the complications; they impose great reserve concerning the late prognosis.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

94:505-572 (Feb. 25) 1950. **Partial Index**

Wilm's Tumors: Malignant Renal Tumors in Children. J. I. de Bruijne.—p. 513.
*Dicumarol Therapy in Cardiac Diseases. W. J. Bruins Slot.—p. 521.

Dicumarol® Therapy in Diseases of Heart.—Bruins Slot treated 16 patients with myocardial infarct with the customary regimen but no dicumarol,® and 21 patients with dicumarol.® Although the proportion of fatal cases was greater in the group treated with the drug, a careful analysis of the causes of death indicate that patients with coronary thrombosis should be treated with this anticoagulant. The prothrombin time should be at least doubled by administration of the drug and should be kept at this level for at least six weeks. Another indication for dicumarol® therapy is the repeated occurrence of cardiogenic embolisms in patients with mitral stenosis or auricular fibrillation. The author cites a patient in whom embolisms originated repeatedly from a rheumatic lesion of the mitral valve. The patient was treated with the anticoagulant for fifteen months, and further embolisms did not occur. The patient recovered to such an extent that she can even climb stairs without difficulty.

Oncologia, Basel

2:193-252 (No. 4) 1949. **Partial Index**

Cancer: Etiology, Prophylaxis and Therapy. O. Bayard.—p. 193.
Stricture of Mesopharynx as Late Change Following Roentgen Irradiation of Cancer of Upper Air and Food Passages. H. Steinmann.—p. 217.
*Eggwhite as Carcinogenic Factor. W. D. Hartmann.—p. 233.

Egg White as Carcinogenic Factor.—Hartmann points out that the role of proteins in the pathogenesis of cancer has been discussed repeatedly. The incidence of cancer is greater in groups whose food contains large amounts of animal proteins and lower in groups with a predominantly vegetarian diet. He investigated the carcinogenic effect of egg white. Fifty guinea pigs were given daily subcutaneous injections of 2 cc. of fresh egg white, and 20 rabbits received injections daily with 5 cc. The first epithelial lesions could be observed after five or six days. The white or whitish gray nodules at first showed no signs of malignancy, but soon carcinomatous cells appeared in the connective tissue stroma. The malignant connective tissue tumor was identified as sarcoma magnifuso cellulare. A perusal of the literature convinced the author that this is the first report on the experimental production of tumors in animals after the application of animal protein.

Prensa Médica Argentina, Buenos Aires

37:355-390 (Feb. 24) 1950. **Partial Index**

*Arterial Hypertension and Conditioned Reflexes. O. de Carvalho.—p. 355.

Arterial Hypertension and Conditioned Reflexes.—De Carvalho says that arterial hypertension is a definite disease which develops through conditioned reflexes elicited by mental, chemical and physical allergic stimulations. The first phase of the disease is a nervous mental disorder created by exogenic reflexes which stimulate the cortical and hypothalamic centers and the hypophysis; this phase develops into a hypertensive cerebropathy. Continuation of subconscious endogenic conditioned reflexes for several months or years results in the production of a splanchnic neurosis which advances into the second phase of arterial hypertension shown by hypertensive splanchnopathy. Persistence of the conditioned reflexes in the presence of hypertensive splanchnopathy leads to arterial neurosclerosis and the advance of the disease into its third stage, irreversible hypertensive arteriopathy. Cerebral hemorrhage in arterial hypertension is produced by a primary, allergic necrobiosis of the cerebral cells, without lesions of the cerebral blood vessels. Necrobiosis results from lack of production of the mimetic substance which controls the dynamics of the cerebral blood vessels from an allergic stimulation of the hypothalamus. Large cerebral hemorrhages from rupture of a large cerebral blood vessel, as for instance the Sylvian artery, are due to angionecrosis secondary to softening of the periarterial cerebral tissues.

Ugeskrift for Laeger, Copenhagen

112:467-500 (April 6) 1950. **Partial Index**

*Low-Salt Diet in Cardiac Insufficiency. A. L. Nielsen, P. Bechgaard and H. O. Bang.—p. 467.
Trichobezoar. J. Ernst and C. Villuame.—p. 474.
Glutamic Acid in Therapy of Schizophrenia. J. Ravn.—p. 477.

Low Salt Diet in Cardiac Insufficiency.—Nielsen and his associates report on 64 cases of cardiac insufficiency with doubtful prognosis in which diet with sodium chloride content of less than 1 Gm. daily was given in combination with the usual methods of treatment. They describe in detail 4 serious cases in which improvement occurred only after transition to the diet low in sodium. During hospitalization there was considerable improvement in 36 patients and less evident improvement in 21; 6 grew worse and died, 1 was unaffected and 2 died from intercurrent disease. Of the 50 patients followed three to eighteen months after discharge, 31 had adhered to the diet. Of these, 27 were unchanged, 1 was less well and 3 had died, 1 from cerebral embolism. Of the 19 patients who had disregarded the diet, in 3 the condition was unchanged and in 11 it was aggravated; 5 had died, all from cardiac insufficiency. In treatment with a low sodium salt diet it is not expedient to limit the fluid intake. Chronic renal disease with constant loss of sodium chloride and Addison's disease contraindicate use of the low salt diet.

BOOK NOTICES

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

The Cytologic Diagnosis of Cancer. By the Staff of the Vincent Memorial Laboratory of the Vincent Memorial Hospital, a Gynecologic Service Affiliated with the Massachusetts General Hospital, Boston, Massachusetts. The Department of Gynecology, Harvard Medical School. Published Under the Sponsorship of the American Cancer Society. Cloth. $6.50. Pp. 229, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London W.C.2, 1950.

This book contains a foreword by Joe V. Meigs and Maurice Fremont-Smith of the Department of Gynecology, Harvard Medical School, and its publication is sponsored by the American Cancer Society. A careful reading of the book indicates that Mrs. Ruth M. Graham, who is presumably the chief technician in the cytologic laboratory of the Vincent Memorial Hospital, is the principal author; one wonders why she did not assume the privileges and responsibilities of authorship.

The book presents the subject of the cytologic diagnosis of cancer by means of an atlas of photomicrographs and drawings and a detailed description of the cells. In each section there is a single black and white photomicrograph of a typical histologic section and a low power and a high power photomicrograph of the cells under discussion as they appear in smears, with a drawing of the high power photomicrograph reproduced in full color. These are excellent for the most part, although sometimes a single photomicrograph of a histologic section is not truly representative, for example, the photograph of squamous cell carcinoma of the cervix on page 41. The findings in the following conditions are well described and pictured: carcinoma of the cervix and endometrium; carcinoma of the genital organs; radiation changes in normal and malignant cells of the vaginal secretion; tumors of the respiratory tract, stomach, urinary tract, pleura and peritoneum. The final chapter discusses technic, and the bibliography is comprehensive.

The authors state that they have not discussed the smears of pregnancy and the postpartum period because this type of material was not available to them. Such a discussion might profitably be added in future editions, since smears taken at this time are often difficult to interpret. There is no statistical information of the accuracy of the method.

The book is probably the best that has been published so far and will prove a valuable reference work in the pathologic laboratory.

Varicose Veins. By R. Rowden Foote. Cloth. $8. Pp. 226, with 181 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Butterworth & Co., Ltd., 4-6 Bell Yard, Temple Bar, London, W.C.2, 1949.

This monograph on varicose veins, by an author of distinction and authority in this field, is well written and profusely illustrated throughout. The importance of this too frequently neglected field is pointed out in the preface, where it is stated that there are probably 5,000,000 sufferers from varicose veins in Great Britain alone. This can be reinterpreted by the reader of this review in terms of the United States.

The author has prepared an excellent historical section, pointing out the importance of varicose veins from the beginning of history and also the recurrent, cyclic return of the surgeons to classic procedures described, in principle at least, repeatedly during the previous centuries. Today, fortunately, with the use of antibiotics and anticoagulants and better surgical technics, there is a great improvement in the immediate and late results from varicose vein surgery. The section on examination and study of the patient is well presented. In the section on treatment, various methods are comprehensively described, with emphasis on the combined high resection of the vein indicated, plus the distribution of sclerosing solutions along the lumen by use of a nutmeg grater type of needle inserted from above and withdrawn as the solution is distributed. This method, with variations, which was very popular in the United States 5 to 10 years ago, seems now to be less popular in this country, and there is a trend toward return to resection and stripping technics. The author, however, is extremely skilled in this form of therapy, and it may be that in his hands the results are the best that can be obtained in varicose surgery. There is an excellent section on ulcerations resulting from varicose veins and venous stasis. The differential diagnosis of various types of ulcers of the leg is discussed, and this is followed by a description of various forms of therapy. It is worthy of note that Foote was definitely opposed to sympathectomy for this condition. More emphasis might well have been placed on the treatment of fungus infections, which so often complicate the healing of varicose ulcers. There is a well presented section on thrombophlebitis and pulmonary embolism. The author emphasizes the importance of anticoagulant therapy in the field of thrombophlebitis and its replacement of surgical intervention for most cases. He also discusses in some detail the correct use of supportive bandages and their application.

This sound, well written book will be of value to all physicians who are confronted with the problem of varicose veins, and this includes all physicians except a few whose limited specialties spare them the need of facing this difficult, important and challenging problem.

Lehrbuch der Inneren Medizin. Von Dr. Ernst Lauda, O. Ö. Professor, Vorstand der I. Medizinischen Universitätsklinik Wien. Band II: Die Krankheiten der Verdauungsorgane. Die Blutkrankheiten. Cloth. $8.10. Pp. 624, with 47 illustrations. Springer-Verlag, Mölkerbastei 5, Wien 1, 1949.

This is the second volume of a three volume manual on internal medicine by the Viennese internist Ernst Lauda. It covers the diseases of the gastrointestinal tract from the mouth to the anus, including the biliary system and the pancreas and, in addition, infections of the peritoneum and diseases of the hematopoietic system. Although there is no preface to this volume, it is obvious from a perusal of the contents that its aim is to present in systematic form a discussion of the different types of disease which may attack each part of the systems covered in the volume. In the case of important organs such as the stomach, liver and pancreas, the description of the clinical manifestations is preceded by a lucid survey of the underlying anatomic and physiologic facts, and there is also a discussion of the various functional and other laboratory tests which are of value in diagnosis. In the consideration of each disease the main stress is on the symptomatology, but the etiology, diagnosis, prognosis and treatment are also briefly but competently reviewed.

The work is written in clear, uncomplicated German, the discussions are logical and informative, and the text indicates that the writer has a wide acquaintance not only with German but also with French, English and American medical literature. The text also indicates that in spite of the restrictions imposed by the last war the writer has kept up to date on the newer medical discoveries.

Needless to say, there could be differences of opinion as to the relative amount of space to be accorded to some of the many conditions which are described. The section on tumors of the mouth, perhaps, although these are mainly of surgical interest, and the discussion of diverticulitis are examples of conditions which would have been more fully discussed in an American work of similar scope. It is also to be noted that here and there American experience would probably differ from that of the author. The statement that the so-called Virchow gland, commonly described as a metastasis from carcinoma of the stomach, is usually a healed tuberculous gland is not borne out by American experience. There is a question too whether so-called arsphenamine (salvarsan®)

hepatitis is not really due to infected syringes rather than arsphenamine. The discussion of sickle cell anemia fails to give credit to J. B. Herrick as the discoverer. But, after all, these are minor matters and do not detract from the fact that the book as a whole is a scholarly work, well written and accurate.

The general makeup of the work is satisfactory. The volume measures 6½ by 9¾ inches and is much less cumbersome than many medical tomes; the paper and typography are excellent, the charts and the illustrations, including roentgenograms and colored pictures of normal and pathologic blood, are well done, and there is a good index. There are no bibliographies. All in all the work can be commended as giving a clear and logical picture of the conditions which it discusses.

Guiding Learning Experience: Principles of Progressive Education Applied to Nursing Education. By Maude B. Muse, R.N., A.M. Cloth. $4.50. Pp. 617. The Macmillan Company, 60 Fifth Ave., New York 11, 1950.

The author of this excellent textbook has had long and wide experience as a public school teacher, graduate nurse and nurse educator. She is known to the vast majority of the nursing profession for her writings and teaching. She might well be called a teacher of teachers. This book is one of a series of textbooks known as the "Macmillan Nursing Education Monographs." This volume deals with teaching problems of classroom and clinical nurse instructors, both in undergraduate and graduate nursing schools. The book is written in four units. Unit I consists of two chapters and deals with the frame of reference of nursing education and covers the educational philosophy which determines educational methods and the various philosophies of progressive education in a profession. Unit II consists of five chapters and deals with the role of principles in progressive education. In this unit, the author's expert knowledge of the underlying principles of psychology as applied to teaching is skilfully expressed. Unit III consists of six chapters and deals with teaching methods appropriate in progressive education. Unit IV consists of two chapters and deals with principles of unit organization. Preceding the text of each unit is a statement of purpose, and at the end of each unit is an exceptionally complete bibliography. In addition, at the end of each chapter is a well selected list of suggested learning activities, as related to the text. In the preface of the book, the author assumes full responsibility for "the selection, correlation, interpretation and application of the educational and psychological principles" expressed and "for their combination and re-statement as teaching-learning principles."

This is a textbook that every nurse educator, student and graduate nurse should read. Other educators in the allied professions would also benefit by reading this excellent book.

Traité des maladies professionnelles. Par Albert Langelez, professeur à l'Université Libre de Bruxelles. Paper. 450 francs. Pp. 624, with 78 illustrations. Editions Desoer, 21 rue Sainte-Véronique, Liège, [n.d.].

This book is an interesting addition to the rapidly multiplying literature on occupational diseases. The six parts deal with illness due to chemicals, illness due to living agents (such as trichinella), illness due to physical influences (such as ionizing radiations), occupational carcinoma, occupational dermatoses and the pneumoconioses. Each condition is discussed systematically as to pharmacodynamics and toxicology, symptomatology, diagnosis, industrial situations involving exposure, and prophylaxis. In some instances a final paragraph suggests treatment, but so vaguely, uncritically and inaccurately that it would seem to be best to omit these passages in future editions. Examples are the recommendation of high doses of ascorbic acid in treating the multiple neuritis of carbon disulfide poisoning (page 186) and of injections of iron and glucose to prevent carcinoma in cases of hemorrhagic cystitis (page 319).

The illustrations are informative. Among the valuable passages that summarize laws relating to certain special occupational hazards, especially interesting is the passage (pages 499-505) stating the international recommendations for protection against roentgen rays and radium. The lack of an index in a book of this character is regrettable; instead, there is a table of contents at the end. In other respects this book is commendable, for it offers an amazing wealth of facts in attractive, readable form.

Public Health Is People: An Institute on Mental Health in Public Health Held at Berkeley, California, 1948. By Ethel L. Ginsburg. Cloth. $1.75. Pp. 241. The Commonwealth Fund, Division of Publications, 41 E. 57th St., New York 22; Oxford University Press, Amen House, Warwick Sq., London E.C.4, 1950.

This is an outline report giving the essentials of an institute held in the summer of 1948 under the joint sponsorship of the California State Department of Public Health and the Commonwealth Fund. This institute was conducted by 8 psychiatrists and 3 pediatricians with psychiatric training, together with 5 public health leaders; these constituted a faculty for 30 health officers who comprised the student body.

The book reports on what psychiatrists, pediatricians and public health workers can learn about people and how people react to various proposals from professional sources, including psychiatric and public health. The book also describes the procedure by which psychiatrists, pediatricians and public health officials adjusted their respective viewpoints to each other in office with ease and smoothness. Great stress is laid on the importance of learning how to work better with people. In the course of this discussion it was emphasized that there must be evidence of personal interest and not merely routine official or professional relations. One psychiatrist emphasized the importance of recognizing that "When you have stopped seeing people as people you had better get busy having your emotional vision refracted. When they all look alike to you you have stopped seeing them at all." Many of the practical problems of health departments in their relations with their clientele were dissected and the probable causes of success or failure evaluated.

This should be an extremely valuable book to anyone who has any dealings with people in groups. That includes not only public health officials but also teachers, clergymen and, in fact, practicing physicians. It is informally and readably put together, and could indeed be the subject of a profitable series of study hours on the part of anyone interested in human relations.

Operative Obstetrics: A Guide to the Difficulties and Complications of Obstetric Practice. By J. M. Munro Kerr, LL.D., F.R.C.O.G., M.D., and J. Chassar Moir, M.A., M.D., F.R.C.S.E., Nuffield Professor of Obstetrics and Gynaecology, University of Oxford. Fifth edition. Cloth. $12. Pp. 948, with 390 illustrations. Williams & Wilkins Company, Mount Royal & Guilford Aves., Baltimore 2, 1950.

This is one of the outstanding books in operative obstetrics in the world. Since the first edition was published in 1908 tremendous changes have occurred in the practice of midwifery; thus it is only fitting that Munro Kerr has collaborated with Chassar Moir so that this textbook may better reflect the modern viewpoint of obstetric practice. However, throughout the book there appear in small print interesting clinical histories and many comments from the rich storehouse of experience of the senior author. These personal gems of obstetric thought add much to the book.

The book deals first and foremost with the diagnosis and treatment of the complications of pregnancy and labor. There are six sections on the following subjects: the management of normal labor; dystocia from faults in the forces, the fetus and the parturient canal; obstetric operations; injuries and accidents to the mother and child. These are discussed fully and beautifully illustrated by numerous illustrations. In most instances key historical references are cited and the experiences of European and American authors are fully utilized. The authors do not hesitate to recommend the best modern procedures and to condemn some of the practices that have been made obsolete by the march of science.

In general the treatment of obstetric complications favored in this book are the acceptable procedures in American teaching centers. Here and there is a note of great reluctancy to part from traditional practices made honorable by time. Although the authors advocate the more liberal use of cesarean section, they still describe difficult forceps deliveries, even the high forceps, and the use of axis-traction forceps to accomplish these operations. The premature induction of labor for contracted pelvis is still debated although it has long been abandoned in this country. A whole chapter is devoted to operations for the enlargement of the pelvic cavity, which in the United States have become of historical interest. The same can be said of accouchement forcé. There is extreme hesitancy in discussion of spinal anesthesia, although great strides have been

made in this field, and it is rapidly acquiring a real place in programs of anesthesia.

These criticisms are truly minor, for the book represents a vast storehouse of good obstetric information and should be valuable to the obstetric specialist as well as to the practitioner who does much work in this field.

Operative Surgery. By Various Authors. Edited by Alexander Miles, M.D., LL.D., F.R.C.S., Consulting Surgeon, The Royal Infirmary, Edinburgh, and Sir James Learmonth, K.C.V.O., C.B.E., Ch.M., Regius Professor of Clinical Surgery and Professor of Surgery, University of Edinburgh. Third edition. Cloth. $8.50. Pp. 559, with 235 illustrations. Oxford University Press, 114 Fifth Ave., New York 11; Amen House, Warwick Sq., London, E.C.4, 1950.

Twenty-four surgeons of the Edinburgh school have condensed into this book a succinct and remarkably complete account of the operative procedures they commonly employ in treating virtually the complete spectrum of surgical diseases, including those of the blood vessels, nerves, bones, joints and tendons, scalp, face and jaws, neck and thyroid gland, chest and breast, intrathoracic and intra-abdominal organs, rectum, bladder and male genital organs, including hernias. Only gynecologic surgery is omitted. So-called minor surgery is included. The coverage is remarkable considering that a generous sized illustration is usually found on every other page. The illustrations are well chosen, of excellent quality and highly informative. Careful consideration is given to preoperative and postoperative care and to choice of anesthetic agents.

True to its title, the volume is entirely "operative," no attention being given to diagnosis, and it achieves its handy size partly by being dogmatic, in that only one procedure is described for the treatment of each condition considered, namely, the one favored by the particular author. Technically, in describing each operative procedure, coverage is not much more detailed than that of the one-volume surgical texts popular in the United States, and the procedures themselves closely correspond with those in common use here.

The volume is obviously primarily for the undergraduate or young graduate student of surgery, especially for one preparing to take a comprehensive examination in operative surgery.

Bridges' Food and Beverage Analyses. By Marjorie R. Mattice, A.B., Sc.M., Assistant Professor of Biochemistry, Graduate School of Medicine, College of Medical Evangelists, Los Angeles. Third edition. Cloth. $5.50. Pg. 412. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1950.

Those who are familiar with the previous editions of this excellent collection of nutritional data and information will welcome the fact that Miss Mattice has enlarged the preceding edition and brought it up to date. The author is well qualified for this task, since she worked with Dr. Bridges in the preparation of the earlier editions and had the responsibility of assembling and checking the many tables of data originally incorporated in the book. Because of the rapid strides being made in the field of human nutrition the need for authoritative data on the many food factors present in a wide variety of foods has become increasingly important. The present volume admirably meets this need.

The current edition has undergone considerable rearrangement to permit emphasis of changing views in the field of nutrition. Several of the chapters present in the previous editions have been deleted and new ones have been added. The section on vitamins has been extensively enlarged and brought up to date. Vitamin B_{12} is included, and there is a short discussion of vitamin interrelationships and antagonisms. The effect of processing on the nutritive value of foods is given careful consideration and the question of goitrogenic foods is introduced. The mineral section now includes sodium and potassium analyses on approximately 500 foods and 150 municipal water supplies. The tables listing the composition and fuel values of alcoholic beverages will prove valuable to many because of the important role these beverages play in the lives of a great proportion of the population. The text and tables are well annotated and an excellent bibliography is included at the end of the book.

The tables presented in this book, along with the accompanying comments, will prove extremely useful to all those concerned with diet formulations and other nutritional problems. The nutritionist and dietitian, as well as the biochemist and student, should certainly include this volume in his library.

Chemical Inventions and Chemical Patents. By Edward Thomas. Cloth. $16.50. Pp. 881. Matthew Bender & Company, Inc., 109 State St., Albany 1; Clark Boardman Company, Ltd., New York, 1950.

This textbook on United States patent law of chemical inventions brings "up to date the substance of the author's prior 'Law of Chemical Patents.'" Stress is laid on the pitfalls confronting a patent lawyer in drawing up applications, in collecting evidence and in conducting litigation, including interferences. In many instances, cases are cited to more than one set of reports. Patent applications for medicinal agents are given several pages. These patents are said to differ from ordinary chemical patents chiefly in that evidence is required for their safety and efficacy. The book gains by the inclusion of some of the author's personal experiences in practicing patent law. The full text of 15 typical patents is printed in an appendix. There is an extensive table of cases and a detailed index. Unfortunately, the work is very bulky because of the heavy paper, the reproduction by a photo-offset process from varityped copy and the stout binding.

Metabolism and Function: A Collection of Papers Dedicated to Otto Meyerhof on the Occasion of His 65th Birthday. Edited by D. Nachmansohn, M.D. Cloth. $7. Pp. 348, with illustrations. Elsevier Publishing Company, Inc., 215 4th Ave., New York 3; 118 Spuistraat, Amsterdam-C, Netherlands, 1950.

This is a reprint of *Biochimica et biophysica acta* (**4**:1-348, 1950) containing 38 original papers on the metabolism and function of muscle and nerve, on the action of drugs and on intermediate metabolism. As they were assembled in honor of Meyerhof, the papers are preceded by a short biography and appreciation of the work of this prominent physiologist.

The section on muscle contains seven papers, chiefly on enzyme systems concerned in muscle contraction. The authors include Hill, Szent-Györgyi and Needham.

The six papers on nerves cover morphology (Schmitt), permeability as related to function (Nachmansohn and Rothenberg), nerve conduction (Gerard and Doty), functional organization of the brain (Himwich) and development of muscle chemistry as related to neurophysiology (von Muralt).

Specificity of amino-acid decarboxylases, glycolysis in pharmacology and pharmacologic specificity are topics of the three papers in the section on drug action. They are by Blaschko, Gemmill, and Meier and Bein, respectively.

It is difficult to select for special mention from among the 22 widely varied contributions on intermediate metabolism. The character of these papers will be gathered from the following short list: Wald on the in vitro interconversion of retinenes and vitamin A, Kalckar on incorporation of purines and pyrimidines into nucleosides and nucleic acid, Wurmser and Filitti-Wurmser on antigen-antibody systems, Ashwell and Dische on metabolism of nucleated red cells, Boyland on abnormal cell division and Lundsgaard on liver metabolic rate.

All the papers contain informative summaries in English, French and German.

Hospital Nursing Service Manual. Prepared by a Committee of the American Hospital Association and the National League of Nursing Education with the Assistance of Stella Goostray, R.N. Paper. $1.50. Pp. 99. National League of Nursing Education, 1790 Broadway, New York 19, 1950.

This is the third edition of this manual; the original appeared in 1936 and was revised in 1942. This work really replaces the former issues and should be considered as a new manual which "emphasizes principles of good hospital nursing service." Hospital administrators, hospital trustees, directors of nursing, nursing school directors, graduate and student nurses will all benefit from a careful study of this manual, which was written by persons with experience in this field. The medical staff of the hospital could profit by reading this excellent presentation. Skilfully written, it takes the reader through the nursing department, its organization and administration, followed by the functions, qualifications and interdepartmental relations of nursing personnel, all pointing to the development of a coordinated nursing service. Finally, the manual describes budgeting, cost accounting, physical facilities, equipment, supplies and administrative devices essential to the conduct of an efficient hospital nursing service. The manual includes an extensive bibliography.

Principles of Medical Statistics. By A. Bradford Hill, D.Sc., Ph.D., Professor of Medical Statistics in the University of London (London School of Hygiene and Tropical Medicine), London. Fifth edition. Cloth. 10s. 6d. Pp. 282, with 13 illustrations. The Lancet, Limited, 7 Adam St., Adelphi, London, W.C.2, 1950.

The fact that five editions of this small book have been published in the past 13 years makes it obvious that it has found wide acceptance. During this period, this volume has come to be regarded by many as a classic. The present edition has been only slightly altered from the fourth. The major addition has been the inclusion of a set of 25 practical exercises designed to assist the reader in determining whether he has grasped the essential principles discussed in the text.

This book is not a complete text on statistics, nor is it meant to be. Rather, it is a discussion of common problems in medicine requiring the assembly and evaluation of data composed principally of numerical observations. By means of lucid explanations, practical examples and a minimum of mathematics, the author leads the student through a variety of experimental and statistical problems and points out not only the "how" but also the "why" of their solution.

The subject matter is carefully chosen for its applicability to medical problems. The question of selection, including bias in samples and the difficulties inherent in the gathering of data by questionnaire, is discussed. The meaning of frequency distributions is clearly explained and the construction of tables and graphs is presented. The chapter on averages. (mean, median and mode) is a fundamental and readable discussion of the most common statistical constants of a sample in use by all who collect and tabulate data. There logically follows a discussion of the variability of observations and the common measures of variability including the standard deviation.

The many problems of sampling, such as the measurement of the variability of means, proportions, the effect of the size of the sample on the error of the mean and the "significance" of the differences between observed proportions or averages, are adequately discussed and well illustrated by practical problems. Two common statistical tests are thoroughly presented, namely, the chi square test and the coefficient of correlation. Of importance to those interested in public health and vital statistics are the chapters on life and survival tables and the calculation of standardized indexes. Common statistical fallacies are also thoroughly discussed. At the end of the book is a chi square table, a very useful glossary of definitions and a set of practical exercises to which the answers are furnished.

Although there are bulkier and more exhaustive texts on medical statistics, there appears to be little doubt that this volume of Dr. Bradford Hill's is still the most useful and most readable for the general medical worker. In the opinion of the reviewer, this volume should be required reading for every medical student and medical research worker.

The Trial of Hawley Harvey Crippen. Edited with Notes and an Introduction by Filson Young. Second edition. Cloth. $3.50; 15s. Pp. 211, with 7 illustrations. William Hodge & Co., Ltd., 86 Hatton Garden, London, E.C.1; 12 Bank St., Edinburgh 1, 1950.

Hawley Harvey Crippen received his medical education at the Hospital College of Cleveland in about 1883. After an association with various London hospitals he returned to the United States and received a diploma as an eye and ear specialist from the Ophthalmic Hospital, New York, in 1885. In 1900 he returned to London as a representative of Munyons, a patent medicine business, accompanied by his second wife, a music hall singer. One evening about ten years later, Mrs. Crippen suddenly disappeared and Dr. Crippen was subsequently found guilty of poisoning her with scopolamine hydrobromide (hyoscine), mutilating her body and burying it beneath the cellar floor of their home.

The introduction to this book, containing a narrative account of the background activities of Dr. Crippen and his wife leading up to the time of the trial, makes interesting reading. The record of the trial itself is rather tedious, as any long question and answer report usually is. It contains something of interest to today's pathologists and toxicologists, however. The testimony relative to scopolamine hydrobromide, its properties, its uses and the tests for its presence, is detailed. Of most interest, possibly, is the testimony regarding a small piece of flesh which, according to the prosecution, came from the deceased's abdomen and contained a scar which the deceased was known to have had as a result of a previous oophorectomy. The conflicting opinions of the medical experts on the questions of whether the piece of flesh came from the abdomen of the deceased and whether it contained a scar, a part of the navel or a simple fold in the skin reminds the reader that problems of medical testimony have existed for a long time.

You and Your Heart: A Clinic for Laymen on the Heart and Circulation. By H. M. Marvin, M.D., and others. Foreword by Paul D. White, M.D. Cloth. $3. Pp. 306, with 2 illustrations. Random House, 457 Madison Ave., New York 22, 1950.

This is a book written by heart specialists for the layman. The physicians had the help of Mr. David Loth of the publisher's staff in producing a well written, authoritative book in simple, nontechnical language. Just what the layman wants to know about his heart and how it may be affected by disease is contained in this volume. A simple diagram of the heart and circulation is used to explain the normal circulation as well as the effects of the common congenital defects. The only other illustration is that of a hypothetic community, showing graphically the various agencies that should coordinate in a rheumatic fever program. The subject matter covers the whole range of heart diseases, but particular emphasis is given to coronary artery disease, rheumatic fever and congenital cardiac defects. The final chapter discusses frankly a number of common misapprehensions and fallacies about heart disease. The reader will find that heart disease does not condemn one to hopeless invalidism. Stress has been placed throughout on the many ways medicine can help the patient with heart disease, even in some few instances curing him completely. This book should do much to counteract the fear of heart disease that fund-raising groups have spread in their otherwise well meaning efforts to obtain money for research in heart disease.

Trastornos del crecimiento y del desarrollo sexual. Por J. M.ª Cañadell, jefe del Departamento de endocrinologia de la Clinica médica "B," Barcelona. Cloth. 75 pesetas. Pp. 233, with 88 illustrations. Publicaciones médicas, José Janés, editor, Muntaner, 316, Barcelona, 1949.

This is a monograph in Spanish representing conferences and communications presented in the medical clinic of the *Facultad de Barcelona* under Prof. M. Soriano and in the pediatric service of Dr. Martínez García of the Santa Cruz y San Pablo Hospital.

The author has attempted with this material to develop concise clinical concepts for the diagnosis and treatment of difficulties in growth processes and in the sexual development of children. The book proceeds from a general discussion of factors affecting growth through a specific consideration of the several classes of growth abnormality with extensive discussion of the hormonal influences and syndromes attendant thereto.

The book is well illustrated and contains a bibliography of 220 references, many of them from English and American literature.

Methods in Medical Research. Volume II. Julius H. Comroe Jr., Editor-in-Chief. Methods of Study of Bacterial Viruses, Mark H. Adams, Editor; Pulmonary Function Tests, Julius H. Comroe, Jr., Editor; Assay of Hormonal Secretions, Eleanor H. Venning, Editor. Cloth. $6.50. Pp. 361, with illustrations. The Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1950.

This is the second volume of an annual series of reviews of methods and technics in medical research. The present volume covers the subjects of bacterial viruses, pulmonary function tests and assay of hormone secretions. In each section a large number of tests are described, and in every instance detailed procedures are given together with an evaluation and discussion of the accuracy, value and limitations of the method. In general, the discussions are critical and valuable. This is a convenient reference for laboratory workers and should save considerable time when one is confronted with the necessity of selecting a particular method of analysis or a particular test to be utilized in a research problem. The book is well indexed and references to original work on the methods described are given.

QUERIES AND MINOR NOTES

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted on request.

INHALATION OF DIETHYLSTILBESTROL

To the Editor:—Two months ago a male chemist aged 30 was exposed for a period of three weeks to dust containing large amounts of diethylstilbestrol. Since then he has been complaining of diffuse, exquisite tenderness of both breasts. Since physical examination, including routine laboratory tests, reveals otherwise normal conditions, what is advised?

Sidney Smedresman, M. D., New York.

ANSWER.—The tenderness of the breasts is undoubtedly related to the inhalation of diethylstilbestrol in dust. The best method of treatment is complete freedom from exposure to the drug. Administration of androgens is not of much value in reducing the size of the breasts in these circumstances.

DOSAGE OF DICUMAROL®

To the Editor:—In a patient with phlebothrombosis, with a prothrombin test of 17 seconds by the Quick method, is 300 mg. of dicumarol® an excessive initial dose?

W. R. Bunge, M.D., Laurel, Md.

ANSWER.—The usual initial dose of dicumarol® in patients with a normal prothrombin time is 200 to 300 mg., depending on the size and condition of the patient. Subsequent doses should not be given until the prothrombin time has been determined. A dose of 100 to 200 mg. may be given on the second and subsequent days, provided the prothrombin activity is 25 per cent or more of normal. In the case mentioned, the prothrombin time is within the limits of normal and 300 mg. of dicumarol® would not be considered an excessive initial dose.

URINARY INCONTINENCE

To the Editor:—Please inform me of the management of urinary incontinence in a 5 year old girl with congenital spina bifida.

M. D., California.

ANSWER.—One needs considerably more data about the patient in order to discuss the problem adequately. A thorough neurologic examination is indicated to determine the extent of the nerve damage, i. e., whether the rectal sphincter or lower extremities are involved. If the nerve damage is extensive, little benefit from neurosurgical procedures on the cauda should be expected. Complete urologic study should be done, including cystoscopy, excretory urograms and cystogram, with close attention being given to the possibility of other congenital anomalies such as extravesical ureteral orifices. In certain cases transurethral revision of the bladder neck will correct incontinence due to a spastic internal sphincter. Little relief can be expected from this procedure if decided atony of the sphincter is present. Mechanical devices for the female with a hopeless incontinence of this type are unsatisfactory. Transplantation of the ureters is questionable if atony of the rectal sphincter exists. I recently saw a patient in her early twenties with a congenital solitary kidney who had cutaneous ureterostomy performed years before for congenital spina bifida. She was married and pregnant.

CHRONIC PROSTATITIS

To the Editor:—Textbooks recommend that treatment of chronic prostatitis be continued until the prostatic smear becomes free from more than 8 to 10 leukocytes per high power field, this being the normal level. If on routine physical examination pus is found in the prostate and if the unconnected basic condition, avitaminosis, is cured, but the prostate keeps on showing pus on massage, is it necessary or proper to keep on treating the prostate?

George Vash, M.D., Aldenville-Chicopee, Mass.

ANSWER.—After recovery from the unconnected basic condition, this patient continues to show pus in the expressed prostatic secretion. It is assumed that other possible foci have been eliminated. Careful cystourethroscopic examination should be performed, with search for possible dilated prostatic ducts, which might contain stones. These frequently would be revealed in roentgenograms of the prostate; one should not continue to massage a prostate without such additional study. If dilated, and infected prostatic ducts, with or without stones, are not found, one might prescribe a week or ten day course of sulfonamide drug, penicillin or other antibiotic, continuing the massage for a month or two. A rest for eight to twelve weeks would then be indicated, after which the prostate should be checked. In the continued absence of symptoms, the prostate should be examined from time to time.

DISCHARGE FROM INFANT'S EYES

To the Editor:—An infant 8 weeks of age has inflammation and white discharge from the eyes mostly at the inner canthus. Silver nitrate was used at birth. Microscopic examination of the discharge showed mucus shreds and a few pus cells but no organisms. Ten per cent mild silver protein solution and boric acid wash did not improve the condition. What is the best treatment for this condition?

Harry Hollorman, M.D., New York.

ANSWER.—It is not clear from the inquiry whether this 8 week old infant has a nonspecific conjunctivitis or dacryocystitis. The best treatment for conjunctivitis is the use of eyedrops with 500 units of penicillin in saline solution, or streptomycin or aureomycin, depending on the causative agent. The following formula for eyedrops has been found to be efficacious:

	Gm. or Cc.
Zinc sulfate	0.016
Boric acid	0.32
Distilled water in sufficient quantity	
To make	30

Massage over the tear duct from above downward may aid in curing the dacryocystitis and secondary infection of the tear duct, though probing may be necessary to correct the condition in many instances.

CORRECTIVE EXERCISES FOR PHYSICAL DEFECTS

To the Editor:—I have a son who is over 6 feet (183 cm.) tall and is narrow chested and underweight, with poor muscular development and a slight scoliosis, which is postural. He is now 19 years of age and will not cooperate for any system of corrective exercises. To what age is it possible for the osseous system to develop, to correct such defects, improve one's build such as enlargement of the thorax, increase lung power and the like?

M.D., Tennessee.

ANSWER.—A person 19 years of age who has these physical defects should be doing corrective exercises, including deep breathing, now, before the centers of ossification of the spine have ceased to grow. Some improvement can take place over the next five years or so. The postural scoliosis may be corrected by raising of the heel on the affected side. If fascial contraction is present in the lower extremities, this factor must be removed. It is important to develop the musculature in order that the patient's posture will not slump from fatigue.

ETHER FOR ANESTHESIA

To the Editor:—Ether is packaged in ¼ pound (0.11 Kg.) cans in two forms: (1) anesthesia ether and (2) U. S. P. ether. Are there any differences between the two ethers which would limit or contraindicate use of U. S. P. ether for general inhalation anesthetics?

John M. Malone, M.D., Portsmouth, R. I.

ANSWER.—"ether for anesthesia," "ether, U. S. P." and "ethyl oxide, U. S. P." are alike in all essentials, and all three can be safely used for anesthesia. If any of these products is packaged in a container holding more than ½ pound (0.23 Kg.), or if a container has been opened more than twenty-four hours, then the product should be submitted to the U. S. P. tests for acidity, for peroxides and for aldehydes, not more than twenty-four hours before its use. If these are absent, the product is safe for anesthesia. The University of Minnesota Hospitals and Minneapolis General Hospital have for many years used the products mentioned, under the foregoing conditions, out of 27 pound (12.2 Kg.) containers without observing any clinical differences. Positive tests for deterioration or contamination products have been extremely rare. When present the batch has been discarded. In 1942 the Council on Pharmacy and Chemistry published a report by Harry Gold (*J.A.M.A.* 120:44 [Sept. 5] 1942) on this subject.

DIAGNOSIS OF SYPHILIS

To the Editor:—In this area, where syphilis is uncommon, I have encountered 2 cases on which I would like advice. A man aged 45 was referred by another physician in 1947 for what had been diagnosed as lupus erythematosus. Recently while visiting in another state he had a Wassermann test, and the serologic reaction was positive. He then told me that his reaction to the Wassermann test was positive six years ago but that he had supposed himself cured after receiving a "ninety day treatment" which had resulted in reversal of the blood reaction. Laboratory data have been as follows: spinal fluid test on June 30, 1948 showed a total protein of 9 mg. per hundred cubic centimeters with 5 cells per cubic millimeter. Serologic test of the spinal fluid was negative, and the Lange gold curve was 1111000000. Results of blood tests were: June 28, negative; July 24, positive, titer not determined; July 28, positive, titer 1:1; November 12, positive, titer not reported, and November 20, doubtful reaction. Treatment has not been given since the date of the last Wassermann test. Recently the patient was found to have a fusiform dilatation of the aorta, which undoubtedly is syphilitic. I would appreciate suggestions on the method of approach to this condition, particularly as to the intensity and method of treatment and what may be expected in the way of results. The second patient is a young man in his early thirties, who has a positive serologic response to the Wassermann test. There is no history of infection, and he has no other signs of the disease. Spinal tap was done without increase in pressure. The total protein was 14 mg. per hundred cubic centimeters; the flocculation test was negative, and the colloidal gold curve was 000000000. Tests on the blood were as follows: Dec. 1, 1949, positive; Jan. 25, 1950, positive, titer 1:16; January 31, positive, titer 1:32, and March 28, positive, titer 1:16. Should the condition of this young man be diagnosed as syphilis? Since he must work every day, is it advisable that his treatment be carried out at home?

Ray S. Wycoff, M.D., Lexington, Neb.

ANSWER.—With the information submitted it cannot be decided whether the 45 year old man with low titer positive serologic tests does or does not have syphilis. Lupus erythematosus, assuming that the patient actually has this disease, is a frequent cause of biologic false positive serologic tests which may persist over a period of years. Fusiform dilatation of the aorta in a man aged 45 does not definitely establish a diagnosis of syphilitic aortitis, since dilatation and tortuosity of the aorta may often be produced by other causes, including arteriosclerosis and hypertension.

The serologic titer in the second patient in his early thirties is suggestive that the patient has syphilis, though it is by no means definite proof. Here too, biologic false positivity is a possibility which must be explored. Biologic false positive serologic reactions divide themselves roughly into two groups, acute and chronic. The acute group is usually readily recognizable on the basis of the following criteria:

(*a*) The patient has been known previously to be seronegative.
(*b*) He has had no reasonable exposure to syphilitic infection, as determined by history.
(*c*) The improbability of exposure is verified by examination with negative results of familial and sexual contacts, including parents, siblings, wife, children and extramarital contacts, if any.
(*d*) There is a verified episode of a known precipitating and infectious cause of biologic false positivity, including, for example, such infections as vaccinia, virus pneumonia, infectious mononucleosis malaria.
(*e*) The patient is known to have become seropositive during such an episode.
(*f*) Physical examination for clinical evidence of syphilis is normal.
(*g*) The blood serologic titer is usually, though not necessarily, low.
(*h*) The spinal fluid is normal.
(*i*) Spontaneous reversal to seronegativity occurs within a period of not longer than six months, in the absence of any antisyphilitic treatment.

Applying these criteria to the 2 patients under discussion, patient 1 does not fit, since he has been known to be seropositive for at least three years. On the other hand, lupus erythematosus or other forms of collagen disease are a common cause of "chronic" biologic false positivity.

As to patient 2, the information supplied is inadequate. Of the factors enumerated, there is no information about (*a*), (*b*), (*c*), (*d*), (*e*) and (*i*). All of these factors should be investigated.

Nelson and Mayer have recently demonstrated that in syphilitic infection two antibodies are produced. One of these is reagin, which reacts with standard beefheart lipoid antigens; the other, distinct from reagin, is an antibody which immobilizes and presumably kills virulent Treponema pallidum. Reagin is actually nonspecific since it, or a substance like it, does occur in minute quantities in the serum of all normal persons, and in increased amounts under the influence of a whole group of extraneous infectious causes not due to treponemal infection. The second antibody, the treponemal immobilizing antibody, is considered specific for the treponematoses, including syphilis. When both tests are positive, the patient may be assumed in the United States to have syphilis. When standard tests are positive, but the treponemal immobilization test is negative, there is strong evidence in such patients as the two described in this query that the positive standard test is biologic false positive in nature. Unfortunately, the treponemal immobilization test is not generally available; it is under experimental study in only two laboratories of the entire country. Finally, if it can be demonstrated that either of these patients has syphilis, rather than a biologic false positive serologic test, treatment may be given on an ambulatory basis with 6 to 10 million units of procaine penicillin G in oil plus 2 per cent aluminum monostearate, administered daily, or every other day, in single intramuscular injections of 600,000 units each.

FUNGOUS INFECTION OF PROSTATE

To the Editor:—A man aged 31 complains of difficulty of urination. He denies having had gonorrhea. Leukocytes and mucous threads were present on repeated examinations. Treatment for assumed gonorrhea was started after the upper half of the right prostate was found to be congested, not painful but rather soft and poorly limited. Repeated smears were negative for gonococci. Notwithstanding the treatment, leukocytes in the urine were persisting as was the congestion of the prostate. After repeated examination a curious sediment of tiny golden yellow flakes with some dark was proved microscopically to show a typical mycelium with hyphae. Penicillin and potassium iodide relieved considerably the difficulty of urination, but leukocytes and mycelium persist after two months of therapy. Kindly advise about treatment.

A. Berzin, M.D., Manila, P. I.

ANSWER.—Fungous infection of the genitourinary organs is rare. It is generally assumed in such infections of the prostate and testis that the fungus is blood borne. Search for the original focus should be made. It is possible that there is a partially draining abscess of the prostatic ducts. Careful examination of the prostatic urethra with the panendoscope should be made; if dilated prostatic ducts are found, indicating an opening of a partially draining abscess, incision with a Collings electrode would be indicated. Intensive treatment with penicillin up to 1,000,000 units a day for several weeks may be effective in a large percentage of cases; penicillin combined with streptomycin, 1 Gm. a day, is effective in some instances. Alternate courses of chloramphenicol or aureomycin have been used with penicillin and streptomycin, with benefit in some instances. Perhaps 15 or 20 per cent of these patients will not be cured by present methods of treatment. One would hesitate to use open surgical drainage of the prostate in a person so young unless the urgency of the situation demanded it.

ANESTHESIA FOR TONSILLECTOMY

To the Editor:—Some anesthetists advocate routine intratracheal anesthesia for tonsillectomy in children as well as adults. What is the consensus on this subject?

M.D., Arizona.

ANSWER.—Choice of anesthesia for tonsillectomy and method of administration must be based on age and condition of the patient, tonsillectomy procedure to be employed, whether or not adenoids are to be removed and whether or not special attention must be given to lymphoid growth in the area of the eustachian orifice, as is true when recurrent episodes of middle ear infection or secretory otitis is a primary consideration. In general, local anesthesia is most desirable if the patient is an adult or is old enough to cooperate completely. For tonsillectomy and adenoidectomy in small children, pharyngeal insufflation of ether by the drop method of induction appears suitable. For larger children and those adults who require general anesthesia, gas by means of a rubber endotracheal tube inserted through the mouth or nose is considered preferable by many surgeons. With this method inhalation of foreign matter may be prevented by maintenance of slight positive pressure during the procedure and by leaving the tube in place until pharyngeal reflexes return.

The use of the head-low position employing the Davis mouth gag, by which the airway can be kept entirely free of foreign matter during the course of the operation, obviates the need for endotracheal tube technic.

HABITUAL ABORTION

To the Editor:—I have a patient who in June 1949 had a spontaneous abortion of about two months. Curettage was done, and she made a normal recovery. She was again pregnant and had a missed abortion of about three months' duration, for which curettage was done two months later, March 1950. She is Rh positive. Five years ago she had brucellosis, which has since recurred at intervals. What is the latest opinion about the role of brucellosis in producing abortions?

Keith B. Preston, M.D., Utica, N. Y.

ANSWER.—It is exceedingly doubtful that brucellosis is responsible for habitual abortion. Comprehensive study at the Chicago Lying-in Hospital of over 50 patients who had at least three consecutive abortions failed to implicate brucellosis seriously. No treatment for this condition is indicated during pregnancy unless an exacerbation occurs.